The Cognitive Effects of Alcohol Hangover

Gunn, Craig

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The Cognitive Effects of Alcohol Hangover

Craig Arthur Gunn

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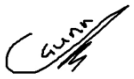
Candidate's signature: 

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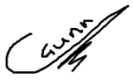
I am the author of this thesis, and the work described therein was carried out by myself personally, with the exception of 4 articles/chapters where 10% of the work was carried out by other researchers (collaboration for the presentation of data in journal format for the studies contained within this thesis).

Candidate's signature: 

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Abstract

Alcohol hangover refers to the combination of symptoms that occur the morning after a night of heavy alcohol consumption, when blood alcohol concentration is approaching zero. Alongside the physical effects of hangover (e.g., headaches, nausea), hangover can negatively affect mood and impair cognition. However, variability in methodological design and low methodological rigour have contributed to mixed results in the literature, preventing firm conclusions about the specific cognitive processes affected by hangover being made. Furthermore, few studies have explored the effect of hangover on attentional bias towards alcohol-related stimuli, response inhibition, emotion regulation, or core components of executive functions.

To investigate the cognitive effects of alcohol hangover in the present thesis, the methodological approaches used in previous research were critically examined and a rigorous methodology that could be utilised in experimental work was developed. This methodology included a within-subject naturalistic design, a-priori sample size calculations and included measures of hangover severity to improve the validity of the hangover condition. A systematic review and meta-analysis of the literature was conducted to provide clarity to the field using the developed methodological approach as guidance for inclusion criteria. Three experimental studies then investigated the effect of hangover on response inhibition and attentional bias toward alcohol-related stimuli, emotion regulation, and core components of executive functions (i.e., switching, updating, and goal maintenance).

Findings from the systematic review and meta-analysis indicated that sustained attention, psychomotor speed, and short- and long-term memory were impaired during hangover. To assess the effect of hangover on response inhibition and attentional bias towards alcohol-related stimuli, participants completed a Go/No-Go task (inhibition) and a Visual Dot Probe task (attentional bias) whilst hungover and during a no-hangover control condition. Results indicated that response inhibition was impaired during a hangover relative to no-hangover, suggesting that individuals are less able to inhibit pre-potent responses during a hangover. However, attentional bias

towards alcohol-related stimuli was unaffected by hangover, which may indicate hangover does not influence attentional biases, but could also be due to the insensitivity of the Visual Dot Probe task. In the second experimental study presented in this thesis, emotion regulation ability during a hangover was assessed using a subjective self-report questionnaire alongside an objective lab-based emotion regulation task. Results somewhat conflicted as participant's perceived greater difficulties in emotion regulation, but the objective lab-based task indicated no difference in emotion regulation ability between hangover and no-hangover conditions. However, it should be noted that the lab-based task did reveal a general negative shift in affective appraisal of stimuli during a hangover relative to the no-hangover condition. The third experimental study in this thesis assessed the effect of hangover on switching, updating, and goal-maintenance using a number-switching task, n-back task (updating), and AX-CPT task (goal maintenance). Results indicated that all three core executive functions were negatively affected by hangover. Overall, these results suggest that core cognitive processes (memory, attention, and psychomotor skills) and higher-order executive functions are impaired during alcohol hangover.

Chapter 1: Introduction

1.1 General Background and Purpose

Alcohol hangover is the most common negative consequence of heavy alcohol consumption and affects between 77-90% of alcohol drinkers (Howland, Rohsenow, & Edwards, 2008; Kruisselbrink, Bervoets, de Klerk, Van de Loo, & Verster, 2017; McGee & Kypri, 2004). Traditionally, definitions of alcohol hangover have varied, but researchers in this area have recently come to the consensus that alcohol hangover refers to "the combination of mental and physical symptoms occurring the morning after a night of heavy alcohol consumption, when blood alcohol concentration (BAC) approaches zero" (van Schrojenstein Lantman, van de Loo, Mackus, & Verster, 2017, pp153). Hangovers typically occur in a dose-dependent fashion, with a positive association between level of alcohol consumption and likelihood of experiencing a hangover (Verster, de Klerk, Bervoets, & Kruisselbrink, 2014). It is estimated that alcohol-related absenteeism, to which hangover is a major contributor, costs the UK economy £1.9 billion per annum (Bhattacharya, 2017), and lost productivity at work due to hangover is thought to cost an additional £1.2 – 1.4 billion per annum (Bhattacharya, 2019). Hangover may also affect every day behaviours, such as driving (Verster, Bervoets, et al., 2014) and relationships with colleagues at work (Ames, Grube, & Moore, 1997), raising concerns for public safety and individual wellbeing.

Relative to other aspects of alcohol research, there has been far less empirical research on hangover. Table 1.1 shows that, although there is greater public interest in hangovers than alcohol intoxication, as indexed by 'hits' in Google, scientific research is 25 times greater in the field of alcohol intoxication, as indexed by 'hits' in PubMed. An important aspect of hangover that could contribute toward its impact on everyday life (e.g., reduced productivity at work) is the effect it has on cognitive processes. In those studies that have investigated cognition during hangover, some have reported no evidence of an effect (Carroll, Ashe, & Roberts, 1964; Chait &

Perry, 1994; Collins, 1980; Collins & Chiles, 1978; Dowd, Wolfe, & Cramer, 1973; Finnigan, Hammersley, & Cooper, 1998; Finnigan, Schulze, Smallwood, & Helander, 2005a; Howland et al., 2010; Ideström & Cadenius, 1968; Lemon, Chesher, Fox, Greeley, & Nabke, 1993; Morrow, Leirer, & Yesavage, 1990; Myrsten, Neri, Kelly, & Rydberg, 1970; Rohsenow et al., 2010; Verster, van Duin, Volkerts, Schreuder, & Verbaten, 2003). However, others indicate alcohol hangover may impair memory (Howland et al., 2010; McCaul, Turkkan, Svikis, & Bigelow, 1991; McKinney & Coyle, 2004, 2007; Verster et al., 2003), attention (Anderson & Dawson, 1999; Howland et al., 2010; McKinney, Coyle, Penning, & Verster, 2012; T. Roehrs, Yoon, & Roth, 1991; Rohsenow et al., 2010), information processing speed (Anderson & Dawson, 1999; Grange, Stephens, Jones, & Owen, 2016), visual and spatial abilities (Kim, Yoon, Lee, Choi, & Go, 2003; Myrsten et al., 1970) and psychomotor abilities (Grange et al., 2016; McKinney & Coyle, 2004, 2007). Inconsistent findings, summarised in Table 1.2, may be due to the vast differences in methodology between studies, differences in the definition of alcohol hangover adopted, or low methodological rigour (Ling, Stephens, & Heffernan, 2010; Prat, Adan, Perez-Pamies, & Sanchez-Turet, 2008; Stephens, Grange, Jones, & Owen, 2014; Stephens, Ling, Heffernan, Heather, & Jones, 2008). The methodology used in alcohol hangover research, and its contribution to inconsistent findings will be discussed further in Chapter Two. Despite the aforementioned body of research indicating cognitive impairments such as memory and attention during hangover, few studies have investigated the effect of alcohol hangover on 'higher' cognitive processes – e.g., executive functions. These processes are particularly important as they are utilised in many everyday behaviours, such as decision making and problem solving. Although there is no universally-agreed upon definition, executive functions are generally referred to as the cognitive processes used when behaviour needs to be controlled, when combining several cognitive processes, or when shifting behaviour (Husain, 2017).

Table 1.1.

Number of Google hits (February 6th 2020) Versus the Number of Scientific Publications, as indexed by Pubmed.

	Google	***Pubmed***
Alcohol	3,550,000,000	949,218
Alcohol Withdrawal	104,000,000	14,601
Alcohol Intoxication	35,000,000	16,839
Hangover	**63,300,000**	**654**

Note. This table is an updated version of comparison between public interest and academic studies for hangover research (for original version see *Verster & Stephens, 2010)*

The main aim of this thesis is to improve understanding of the cognitive effects of alcohol hangover. This will be achieved by first developing rigorous methodology that addresses some of the limitations of previous approaches (Chapter Two), which will be adopted in the subsequent experimental studies described in this thesis. The experimental chapters will then address four main aims: 1) to provide clarity to the literature via a systematic review and meta-analysis (Chapter Three); 2) to investigate the effect of hangover on response inhibition and attentional bias towards alcohol-related stimuli (Chapter Five); 3) to investigate the effect of hangover on emotion regulation (Chapter Six), and 4) to investigate the effect of hangover on core components of executive functions (switching, updating, and goal maintenance; Chapter Seven).

1.1.1 Thesis Structure

The current chapter will introduce the theoretical background that the thesis will draw on, discussing how aspects of an alcohol hangover (e.g., physiological effects) could influence cognitions that will be investigated in later chapters. The current chapter will also outline models and previous research that this thesis will address using experimental work, namely the influence of alcohol hangover on cognitions important for everyday behaviours that utilise executive functions, and components of executive

functions. Chapter Two will then discuss the methods used in previous alcohol hangover research, with focus on the contribution of low methodological rigour, inconsistent definitions of alcohol hangover, and wide variation in methodological design to the mixed findings reported on the cognitive effects of alcohol hangover. Chapter Two will also outline the application of a methodological approach that addresses limitations of previous research methodology. Chapter Three will then present a systematic review of the literature examining the cognitive effects of alcohol hangover using criteria based on methodological rigour and an academically agreed definition of hangover. The chapter will synthesise results in a meta-analysis to determine an 'overall' effect of alcohol hangover on cognitive function. The thesis will then go on to investigate the effects of alcohol hangover on attentional bias towards alcohol-related stimuli and response inhibition (Chapter Five), emotion regulation (Chapter Six), and components of executive functions (Chapter Seven) in a series of experimental studies.

1.2 Theories and Explanations of Hangover-Related Impairments

There are several explanations for how cognition may be impaired when experiencing alcohol hangover. Broadly, these can be categorised into energetic factors, physiological effects, psychopharmacological effects, and the symptoms of a hangover.

1.2.1 Energetic Factors

Exerting effortful cognitive control carries an intrinsic subjective cost (Botvinick & Braver, 2015). Limited resource-models argue that this cost is the expenditure of mental resource, whereby over-expenditure can lead individuals to a state in which they no longer have sufficient resource to engage in effortful processing – i.e., ego-depletion (Baumeister & Vohs, 2018). Other models, such as reward-based decision making, posit that effort attenuates reward (i.e., rewards are experienced as less positive the greater the effort needed to achieve them; Botvinick, Huffstetler, & McGuire, 2009). Cognitive Energetics Theory, on the other hand, uses a force-field metaphor

to describe the interplay between a 'driving force' and a 'restraining force' – the sum of which determines the motivation of an individual to engage in effortful cognition (Kruglanski et al., 2012). Although the means by which effort is conceptualised differs between these theories, they all agree that if a task becomes too effortful then an individual's motivation shifts away from the task toward processing salient information or engaging in leisure activities. A recent study of driving ability during hangover that included a rating scale of mental effort found that individuals performed poorer whilst hungover and rated the driving task as more effortful compared to a no-hangover control (Verster, Bervoets, et al., 2014). The additional mental effort needed for task performance during hangover implies individuals are more likely to shift priorities and motivation away from effortful processes whilst experiencing a hangover. This could result in poorer performance or reduced efficiency. Instead, individuals may be motivated to switch away from effortful cognitive tasks toward more salient and restful activities, such as staying in bed to watch movies (Griffin, Freeman, Adams, & Smith, 2018).

Arousal and activation (physiological readiness to respond) contribute to effort as they increase the individual's energy levels to prepare them to meet task demands. Low levels of arousal can influence early information-processing, leading to slower reaction times or accuracy deficits and poorer abilities to sustain attention (Nigg, 2005). Similarly, alertness, time of day, and the consumption of substances can influence the physiological readiness of individuals to respond or process information (Sergeant, 2005). Data from hangover studies indicate low levels of arousal the morning after a night of heavy drinking. For example, several studies have reported reduced alertness levels when experiencing a hangover compared to a no-hangover condition (Finnigan et al., 1998; McKinney & Coyle, 2006; Verster et al., 2003). Hangover also increases fatigue – an indication of low arousal levels (Chait & Perry, 1994; Myrsten et al., 1970) – and sleepiness (Rohsenow et al., 2010), highlighting a negative impact on arousal levels.

In sum, it is likely that individuals experiencing a hangover have low arousal and find tasks more effortful and demanding, which could increase the likelihood of their behaviour becoming more stimulus/externally driven.

1.2.2 Physiological

Heavy alcohol consumption and alcohol hangover lead to physiological disturbances that exert a negative effect on cognition (e.g., dehydration, low blood sugar). Hangover-related increases in the renin-aldosterone axis, involved in water retention, electrolyte regulation, and overall homeostasis, contribute to dehydration (Linkola, Fyhrquist, Nieminen, Weber, & Tontti, 1976; Linkola, Fyhrquist, & Ylikahri, 1979). Elevated vasopressin has also been observed during alcohol hangover, further indicating that individuals are dehydrated the morning after a night of heavy alcohol consumption (Linkola, Ylikahri, Fyhrquist, & Wallenius, 1978). As dehydration can impair visuomotor, psychomotor, short- and long-term memory, and attentional processes (Grandjean & Grandjean, 2007), it is possible that these cognitions are influenced during hangover. Low blood sugar in hangover, resulting from the metabolic state of the liver and other organs in response to alcohol (Vartia, Forsander, & Krusius, 1960; Ylikahri, Leino, & Huttunen, 1976), could also negatively affect mood and memory (Benton, 2001).

Following alcohol consumption, individuals exhibit disrupted biological rhythms, such as shorter, less efficient, and poorer quality sleep (Roehrs et al., 1991; Rohsenow et al., 2010; van Schrojenstein Lantman, Roth, Roehrs, & Verster, 2017). Sleep disturbances contribute to cognitive impairments, specifically in working memory, attention or perceptual processing, and short-term memory (Chee & Chuah, 2007). A meta-analysis exploring the overall cognitive effects of short-term sleep deprivation found impairments in simple and complex attention, processing speed (e.g., reaction times), working memory, and short-term memory (Lim & Dinges, 2010). The cognitive impairments observed in studies of sleep deprivation may also

occur during alcohol hangover, following alcohol's disruptive effects on sleep (Rohsenow et al., 2010).

Other physiological factors involved in hangover include altered immune system activity. Following suggestions of a link between alcohol hangover and cytokine functions (Weise, Shilipak, & Browner, 2000), researchers have investigated how hangover may influence immune function (Kim et al., 2003; A Van de Loo et al., 2015). Kim et al. (2003) measured alcohol and cytokine concentrations from blood samples taken before participants (n = 20) were administered 1.5g/kg (~13 units) of alcohol, and the following morning, 13 hours after consumption. Relative to a no alcohol control condition, there were significant increases in some variants of Interleukin (IL-10, IL-12), and Interferon-γ (IFN-γ) in the hangover condition, indicating that hangover is related to changes in immune reactivity. Interestingly, concentrations of IL-12 and IFN-γ positively correlated with total hangover scores. Other studies have also observed increases in IL-2, IL-4, IL-5, IL-6, IL-10, IFN-γ and TNF-α during hangover (Van de Loo et al., 2015), with IL-6 and IL-10 concentrations related to decreasing hangover symptom severity (Kim et al., 2017). Although the role of most of these cytokines in cognition is unclear, there is research that links IL-6 and TNF to learning and memory in animal studies. Over-expression of IL-6 may impair memory formation and consolidation by influencing neurogenesis (Vallières, Campbell, Gage, & Sawchenko, 2002), and overexpression of TNF may impair learning and memory by influencing synaptic plasticity (Aloe et al., 1999). There is also evidence that IL-2 may be linked to spatial working memory and planning abilities, and IFN may be linked to learning and memory (for a review see McAfoose & Baune, 2009). Furthermore, a recent review of physiological factors associated with hangovers indicates that the changes in immune function during hangover may contribute to cognitive and mood impairments the morning after a night of heavy alcohol consumption (Tipple, Benson, & Scholey, 2017).

Cortisol, a marker of the stress response that is related to hypothalamic-pituitary adrenal axis (HPA) activation, is elevated in both acute intoxication (Cicero, 1981), and hangover (Linkola et al., 1979; Wiese, McPherson, Odden, & Shilpak, 1993). Elevated cortisol combined with findings of elevated blood pressure, pulse, and heart rate (Kupari, 1983; Myrsten et al., 1970) has led to the suggestion that alcohol hangover is a state of physiological stress. Furthermore, hangover may make it difficult to cope with additional psychological stress. McKinney and Coyle, (2007) asked participants to complete cognitive tasks with or without an additional stressor (white noise) the morning they were experiencing a hangover. They found impaired memory and psychomotor performance in the hangover condition relative to a no-hangover and no-noise control. However, when participants were experiencing a hangover and were exposed to an additional stressor these impairments were amplified. Importantly, the stressor only resulted in poorer performance when participants were experiencing a hangover, suggesting that individuals had fewer cognitive resources to cope with the additional stressor during alcohol hangover. Stress is known to impair cognition and mood (Het, Ramlow, & Wolf, 2005; Lupien, McEwen, Gunnar, & Heim, 2009). Furthermore, when stress and sleep deprivation are combined (reflecting aspects of hangover), impairments in attention, memory, and psychomotor performance occur, and negative aspects of mood, such as depression, are increased (Lieberman, Tharion, Shukitt-Hale, Speckman, & Tulley, 2002). Stress also interacts with elements of the immune system, such as increasing IL-6 concentrations, which in turn could influence cognition and mood (Steptoe, Hamer, & Chida, 2007).

Together these data highlight that physiological alterations, such as increased stress, disturbed sleep, and disturbances in immune functioning could contribute toward poorer cognitive ability and low mood during hangover.

1.2.3 Psychopharmacological

Glutamate and γ-aminobutyric acid (GABA) are neurotransmitters that predominantly moderate the balance of neural inhibition and excitation, and are both influenced by the consumption of alcohol (Swift & Davidson, 1998). Acute alcohol intoxication downregulates glutamatergic receptor activation, whilst upregulating GABAergic transmission (Clapp & Bhave, 2008), which could exert a global effect on executive functioning (Stock & Beste, 2014). However, acute alcohol withdrawal (i.e., the first week post-alcohol for alcohol-dependent patients) results in an upregulation of glutamatergic transmission and downregulation of GABAergic transmission (Koob, 2011). Although hangover is different to withdrawal, it has been argued that GABAergic and glutamatergic neurotransmission may be unbalanced whilst these systems are regaining homeostasis following acute alcohol intoxication (Swift & Davidson, 1998). As cognitions such as response inhibition, switching and response monitoring rely on a balance between GABAergic and glutamatergic neurotransmission (Stock & Beste, 2014), it is possible that neurotransmitter imbalance in hangover influences cognitions (including executive functions) and mood.

Some catecholamines, such as dopamine, are upregulated during acute intoxication (Clapp & Bhave, 2008). At high or low concentrations, these catecholamines can have a detrimental effect on cognitive functions reliant on prefrontal cortex (PFC) activity, such as executive functions (Arnsten & Li, 2005). Few studies have explored the effect of alcohol hangover on these neurotransmitters, but some have suggested increased dopamine could persist to the hangover period via the action of acetaldehyde (Correa et al., 2012; Stock, Hoffmann, & Beste, 2017; Wolff, Gussek, Stock, & Beste, 2016). When alcohol (ethanol) enters the body, it is metabolised by the enzyme alcohol dehydrogenase into acetaldehyde, which in turn is metabolised by the enzyme acetaldehyde dehydrogenase into acetate. However, it should be noted that, whilst the rise in acetaldehyde concentration following heavy alcohol consumption is thought to lead to symptoms of hangover (Swift & Davidson, 1998; Weise et al., 2000),

acetaldehyde is almost entirely eliminated during the hangover phase (H. Kim et al., 2017; Prat, Adan, & Sanchez-Turet, 2009; Ylikahri, Huttunen, Eriksson, & Nikkila, 1974). Animal studies exploring brain reward thresholds in alcohol hangover indicate that, unlike acute intoxication, dopaminergic activity decreases in hangover. Schulteis and Liu, (2006) administered a high dose of ethanol (2.0 g/kg) to rats and observed an increase in brain reward thresholds, which may reflect decreases in dopaminergic activity in the medial frontal system (Koob, 2013). Reduced reward positivity in the medial frontal system during hangover has recently been observed in humans, resulting in poorer overall performance in a learnable gambling task (Howse, Hassall, Williams, Hajcak, & Krigolson, 2018). This research suggests that dopamine related neuronal activity could be affected by hangover, which in turn could have an adverse effect on cognitive performance. Higher reward thresholds in hangover would increase the cost relative to reward for an individual and possibly reduce motivation for engaging in effortful behaviour, as suggested by reward-based decision making models (T. S. Braver, Paxton, Locke, & Barch, 2009). Cognitive control is thought to be a domain of reward-based decision making, where goals are updated and managed based on dopaminergic modulation of PFC activity (Botvinick & Braver, 2015; Todd S. Braver, 2012; Todd S Braver, Gray, & Burgess, 2007). Therefore, increased reward thresholds in hangover could reduce the effectiveness and efficiency of cognitive performance.

Acute withdrawal also engages stress modulation and increases norepinephrine levels to overcome the effects of a drug (Koob, 2011). States of acute stress can contribute to increases in norepinephrine levels in the PFC (Arnsten & Li, 2005). As highlighted in section 1.2.2, hangover resembles the effects of stress, or makes one more susceptible to stress. Although few studies have explored the role of norepinephrine during hangover, there is evidence to suggest that levels are elevated (Maki et al., 1998; Myrsten, Rydberg, Lamble, Idestrom, & Lamble, 1980). High levels of norepinephrine contribute to impaired PFC mediated cognition (Arnsten and Li, 2005; Robbins & Arnsten, 2009), such as selective attention, working

memory (Tipple et al., 2017), emotion regulation (Ochsner, Silvers, Buhle, & Longfellow, 2012), attentional control (X. Liu, Banich, Jacobson, & Tanabe, 2004), and inhibition (Aron, 2003, 2007; Aron & Poldrack, 2006; Chambers et al., 2006). Given increased levels of norepinephrine during hangover, these cognitions may become impaired the morning after a night of heavy alcohol consumption.

1.2.4 Symptoms

The physiological alterations associated with an alcohol hangover can give rise to a complex plethora of symptoms experienced the morning after a night of heavy alcohol consumption. When developing scales to measure hangover, studies have identified many commonly experienced symptoms that contribute independently to cognitive impairments (Hogewoning et al., 2016; Penning et al., 2013; Penning, McKinney, & Verster, 2012a; Rohsenow et al., 2007).

Fatigue is the most commonly reported hangover symptom, occurring in 95% of individuals (Penning et al., 2012a). Abd-Elfattah, Abdelazeim, and Elshennawy (2015) posit that physical fatigue induced by exercise exerts an inverted U shape effect on cognition, where moderate intensity and duration provide a beneficial effect, but prolonged physical exercise contributes to cognitive impairment. They highlight that fatigue impairs memory, psychomotor abilities, and the ability to complete dual tasks due to a reduction in available mental resource. Similarly, mental fatigue can induce impairments in cognitions, particularly those that involve attentional control, such as task switching and planning (Linden, Frese, & Meijman, 2003), response inhibition (Lim, Wu, Wang, Detre, & Dinges, 2011), goal-directed attentional selection (Boksem, Meijman, & Lorist, 2005), and sustained attention (Guo, Chen, Zhang, Pan, & Wu, 2016). It is not clear whether hangover produces mental or physical fatigue, but with symptoms including muscle aches and concentration problems, it may be that both aspects are affected the morning after a night of heavy alcohol consumption.

Interestingly, the effects of fatigue on cognitive ability has been discussed in terms of reward-cost trade-offs (Boksem, Meijman, & Lorist, 2006; Boksem & Tops, 2008; van der Linden, 2010). When individuals are experiencing fatigue, they weigh up the potential reward of exerting additional effort to complete the task against the cost of that effort. If the cost is too great, then motivation is shifted away from the effortful task, however if the reward outweighs the cost, then motivation is engaged and effort is exerted. This concept is similar to the force-field metaphor adopted by cognitive energetics theory (Kruglanski et al., 2012), whereby the weight of the driving force (reward) and restraining force (cost) determine engagement in effortful processes (Botvinick & Braver, 2015). As we have seen in section 1.2.3, increased reward thresholds and reduced reward positivity during hangover indicates that the threshold for which reward would outweigh cost would be greater when an individual experiences a hangover. This in turn could shift motivation away from engaging in effortful cognitive processing, instead shifting towards less effortful tasks or leisure activities

Pain, such as headache, stomach pain, or muscle cramps, is also frequently experienced during hangover. Pain can impair many cognitive functions, including memory, psychomotor skills, attention, and general cognitive functions (see Moriarty, McGuire, & Finn, 2011). Pain consumes attention (Eccleston, 1995), which can leave an individual with fewer resources available to engage in cognitive processing, suggesting that hangovers could reduce cognitive resource. Indeed, an EEG study found lower P3 amplitude during a switching task whilst hangover (Wolff et al., 2016), which is thought to reflect reduced availability of attentional resources (Chua et al., 2014; Kida et al., 2004). With hangover consisting of a combination of symptoms (van Schrojenstein Lantman, van de Loo, et al., 2017), where fatigue and pain can be present simultaneously, the resulting resource depletion could influence the balance of the reward-cost trade-off leading an individual to shift motivation away from effectively or efficiently engaging in effortful cognitive

processes, such as executive functions. Furthermore, hangover includes the experience of affective symptoms, such as anxiety and depression, which are known to negatively influence cognition. According to attentional control theory, anxiety reduces attentional control processes, which in turn can impair switching, updating, inhibition, and information processing efficiency (Eysenck, Derakshan, Santos, & Calvo, 2007).

To summarise, energetic, physiological, and psychopharmacological alterations, alongside symptoms of a hangover could influence the individual's capacity to engage cognitive processes. Cognitive processes could become impaired, or an individual's motivation may shift toward leisure or salient information processing. It is therefore likely that cognitive processes, such as learning and memory, psychomotor skills, processing speed, attention, inhibition, and other executive functions are negatively influenced the morning following heavy alcohol consumption.

1.3 The Cognitive Effects of Alcohol Hangover

Compared to research that has examined the influence of other aspects of alcohol consumption on cognition (e.g., acute intoxication, alcohol withdrawal), few studies have explored the cognitive effects of alcohol hangover (Table 1.1). The studies that have been conducted in this field have often differed in their definition of a hangover and methodological approach (see Chapter Two for a detailed discussion). Consequently, there are currently mixed findings regarding the cognitive effects of alcohol hangover, which makes it difficult to derive clear conclusions from the literature.

1.3.1 Psychomotor Skills

Psychomotor skills refer to activities involving movement associated with mental processes and are typically measured by measuring reaction time (RT) to the presentation of a stimulus. Studies investigating the effect of

alcohol hangover on psychomotor skills have reported mixed results. Although there are a number of studies that report null effects (Collins, 1980; Collins & Chiles, 1978; Lemon et al., 1993; Myrsten et al., 1970), others have reported slower psychomotor speed (Grange et al., 2016; McKinney & Coyle, 2004, 2007) and poorer accuracy (Kruisselbrink, Martin, Megeney, Fowles, & Murphy, 2006) the morning after a night of heavy alcohol consumption. It is possible that differences in methodological design may contribute to these mixed findings, particularly as impairments tend to be in more recent studies, where measures have been improved and become more developed (e.g., older studies measured RT in seconds, whereas modern computerised tasks can measure RT in milliseconds). In addition, studies observing reduced psychomotor speed tend to utilise a naturalistic design (participants engage in usual drinking behaviours for the hangover condition), as opposed to the experimental approach (in which a set amount of alcohol is administered under controlled conditions; see Chapter Two for a detailed description).

In the context of time versus accuracy when responding to stimuli in RT tasks, time taken to respond can indicate processing efficiency, with more time indicating poorer efficiency (Eysenck et al., 2007). Slower RTs observed during hangover may imply poorer information processing efficiency. Indeed, Grange et al. (2016) applied diffusion model analysis to investigate which aspects of information processing were influenced the morning following a night of heavy alcohol consumption. They found reduced information processing efficiency and more cautious responding in the hangover condition compared to no-hangover. Furthermore, Anderson and Dawson (1999) also found decreased information processing speed during hangover using cancellation tests, where participants strike-out target stimuli from a list (e.g., Es in a list of non-target letters). These results suggest that hangover impairs the efficiency and speed with which information is processed, which in turn may increase the amount of resource needed to complete cognitive tasks. Thus, fewer resources may be available for other cognitive processes in hangover, creating a similar situation to that of high cognitive load (Lavie, 2010; Lavie, Hirst, de Fockert, & Viding, 2004).

1.3.2 Attention

Sustained attention refers to the ability to focus on an activity or stimulus over a period of time. Sustained attention is typically measured in a task that presents participants with a string of stimuli and participants are instructed to respond when a target appears (e.g., press a key when three odd numbers appear consecutively). Like other aspects of cognition during hangover, studies measuring sustained attention have produced mixed results. Some studies have reported evidence of an impairment during hangover (Anderson & Dawson, 1999; Howland et al., 2010; McKinney, Coyle, Penning, et al., 2012; Rohsenow et al., 2010), whereas others report no evidence of an effect (Collins & Chiles, 1978; Finnigan et al., 1998, 2005a; Ideström & Cadenius, 1968; Myrsten et al., 1970). The mixed nature of results makes interpretation of findings difficult, however null results may reflect methodological limitations of the studies, such as the confounding factor of nicotine consumption in older studies and more recent studies including more developed measures. Nicotine can have a cognitive enhancing effect that may offset any hangover-related impairments (Levin, McClernon, & Rezvani, 2006; Stephens et al., 2014, 2008; see Chapter 2 for further details). Despite the mixed results, it is possible the symptoms of a hangover (e.g., fatigue) give rise to impairments observed in sustained attention (see section 1.2.4).

Divided attention, the performance of two or more tasks at the same time, is often measured using dual-task paradigms such as tracking an object with a joystick with an additional RT task and appears to be unaffected by hangover (Carroll et al., 1964; Chait & Perry, 1994; Collins, 1980; Collins & Chiles, 1978; Devenney & Verster, 2019; Finnigan et al., 1998, 2005a; Lemon et al., 1993; McKinney, Coyle, Penning, et al., 2012). However, some studies have been limited by low sample sizes (*ns* = 5 – 14) or included uneven group sizes in between-subjects designs (Carroll et al., 1964; Chait & Perry, 1994; Collins, 1980; Collins & Chiles, 1978; Finnigan et al., 2005a; Lemon et al.,

1993), indicating low statistical power and poor reliability (Button et al., 2013). Impairments in divided attention following a night of heavy alcohol consumption have been reported (Roehrs et al., 1991); however, as mentioned above, the very small sample size (n = 5) casts doubt on the reliability of this result. One study that appears methodologically rigorous (McKinney, Coyle, Penning, et al., 2012) reported trend-level evidence of a hangover-related impairment on divided attention ($p = 0.054$). As the central executive, the cognitive control component of the working memory model (Baddeley, 1996), is responsible for divided attention further clarity is needed as to how hangover may influence these processes.

1.3.3 Memory

Studies that have explored the effects of hangover on memory have typically examined short-term memory (STM) and long-term memory (LTM). STM is conceptualised as immediate recall following the learning of items, such as a list of words or numbers (Gabrieli, 1998). STM is an important cognitive component as it is highly related (but conceptually separate) to the more complex cognitive processes of working memory (i.e., information processed by the central executive; Engle, Tuholski, Laughlin, & Conway, 1999). LTM, on the other hand, is a theoretically limitless store that holds learned information, which can be retrieved into a 'short-term store' where information can be maintained and manipulated by working memory to accomplish a task.

To our knowledge, there are eleven studies that have analysed STM during hangover, with mixed results reported (Chait & Perry, 1994; Collins & Chiles, 1978; Devenney, Coyle, & Verster, 2019; Devenney & Verster, 2019; Finnigan et al., 1998, 2005a; Howland et al., 2010; McKinney & Coyle, 2004, 2007; Rohsenow et al., 2010; Verster et al., 2003). Several of these studies have reported no evidence of hangover-related effects (Chait & Perry, 1994; Collins & Chiles, 1978; Finnigan et al., 1998, 2005; Rohsenow et al., 2010; Verster et al., 2003), whereas others have reported impaired STM during

hangover (Devenney et al., 2019; Devenney & Verster, 2019; Howland et al., 2010; McKinney & Coyle, 2004, 2007). Interestingly, Howland et al. (2010) reported impaired STM during hangover in female participants only, indicating these effects may be subject to individual differences. However, another study found no evidence for gender differences (Verster et al., 2003). As with many other aspects of cognition, it has been argued that the mixed results reported above could be explained by methodological differences and the limitations of these studies. These limitations include differences in methodological design, the amount of alcohol consumed, validity of the hangover condition, BAC at testing, and small sample sizes (Prat et al., 2008; Stephens et al., 2014; see chapter two for further details).

LTM, on the other hand, has been explored in comparatively few studies (Howland et al., 2010; McKinney & Coyle, 2004, 2007; Verster et al., 2003). Three studies asked participants to learn words from a list whilst experiencing a hangover, followed by delayed recall or delayed recognition. They all reported impairments in the hangover condition compared to the no-hangover condition (McKinney & Coyle, 2004, 2007; Verster et al., 2003). However, Howland et al., (2010) reported no evidence of an effect on an academic quiz performance during hangover when learning took place whilst participants were sober and given an hour and a half to commit the information to memory. Arguably, this learning time allowed for rehearsal and other techniques to enable easier retrieval. However, it is possible that encoding, the process of transferring information into LTM, is impaired by hangover as opposed to the retrieval of information. This is highlighted by evidence of impairments from studies where participants learned information whilst hungover (McKinney & Coyle, 2004, 2007; Verster et al., 2003) as opposed to no evidence of an effect when participants learned information sober but were tested when hungover (Howland et al., 2010). Impaired encoding during hangover may also explain impairments in STM, as participants completing these tasks would also learn information whilst experiencing a hangover.

1.3.4 Executive Functions

Executive functions refer to the cognitive processes used controlling behaviour, combining several cognitive processes, or when shifting behaviour (Husain, 2017). The biological and psychological effects of a hangover (see section 1.2) indicate executive functions may be influenced the morning after a night of heavy drinking. However, few studies have investigated the effects of hangover on higher-order cognitive processes, and there has recently been an increased call to explore the effects of hangover on executive functions (Ling et al., 2010; Prat et al., 2008; Stephens et al., 2014, 2008).

Previous studies have assessed the effect of alcohol hangover on working memory tasks (Chait & Perry, 1994; Howland et al., 2010; Rohsenow et al., 2010). Chait and Perry (1994) used a backward digit-span task to explore the hangover effects of alcohol compared to marijuana. They reported an interaction effect of Alcohol X Marijuana X Time-of-Day, however post-hoc analysis showed no significant differences among conditions. In other studies, Howland et al., (2010), and Rohsenow et al., (2010) used auditory-span backwards, visual-span backwards, and the adaptive paced auditory serial addition test (APASAT). The auditory and visual-span backwards tasks present a string of stimuli (either auditory or visually) and participants are instructed to recall the stimuli in the reverse order of presentation (i.e., if presented 1, 2, 3, then need to recall 3, 2, 1). The APASAT presents a string of numbers and participants are instructed to add numbers orally. Howland et al. (2010) reported an impairment during hangover in the visual-span backwards task; however, there was no evidence of an effect on auditory-span backwards or APASAT tasks. Thus, although there is a need for greater clarity, there are some indications that hangover negatively affects working memory performance. Furthermore, recent studies have indicated that cognitive processes that rely on executive functions, such as prospective memory (Heffernan, 2018; Heffernan, Samuels, Hamilton, & McGrath-

Brookes, 2019), verbal semantic memory (Heffernan et al., 2019), spatial working memory (Devenney et al., 2019), and reward learning (Howse et al., 2018) are impaired during hangover.

One cognitive process that is often thought of as a key executive function is inhibitory control. Some studies have investigated the effect of hangover on interference control – the ability to prevent extraneous stimuli interrupting ongoing cognitive processes. One early study measured interference control using the Eriksen Flanker and Stroop tasks and found that hangover increased interference relative to a no-hangover control (McKinney, Coyle, Penning, et al., 2012). Impaired interference control (as measured by the Stroop task) has recently been replicated in student and non-student samples (Benson, Ayre, Verster, & Scholey, 2018; Devenney et al., 2019; Devenney & Verster, 2019). However, other studies using the Eriksen Flanker task have not replicated these results (Devenney et al., 2019; Devenney & Verster, 2019; Zink, Bensmann, Beste, & Stock, 2018). Further, a recent experimental study indicated that response inhibition (the ability to withhold a pre-potent response) is unaffected by hangover, although response selection may be impaired (Opitz, Hubert, Beste, & Stock, 2019). As with other aspects of cognition (e.g., psychomotor skills, see section 1.3.1) it is possible that factors associated with the design of a study (e.g., greater alcohol consumption in naturalistic designs) influences the ability to observe hangover-related effects. Therefore, greater clarity is needed using a robust methodological approach that increases our ability to observe hangover-related impairments.

1.3.4 Summary

To summarise, there is evidence that hangover influences cognitive processes, but often studies have produced mixed results, possibly due to methodological variability. This variability, which will be discussed in greater detail in Chapter Two, includes different definitions of hangover, different designs (naturalistic vs experimental), small sample sizes, the sensitivity of

outcome measures, and different levels of alcohol consumed. The aims of this thesis are to provide clarity to the mixed literature by conducting a systematic review and meta-analysis (Chapter Three) and to conduct several well-designed experimental studies to address gaps in the literature (Chapters Five, Six, and Seven). The experimental work aims to investigate the effects of alcohol hangover on executive functions that are important for everyday behaviours. Specifically, to investigate the effects of alcohol on response inhibition and attentional bias towards alcohol-related stimuli (Chapter Five), to investigate the effects of alcohol hangover on emotion regulation (Chapter Six), and to investigate the effects of alcohol hangover on core components of executive function processes, namely; switching, updating, and goal-maintenance (Chapter Seven).

Table 1.2. *Summary of the Number of Studies and their Main Findings for the Effect of Alcohol Hangover on Cognitive Performance.*

Author	Method	Design	Alcohol	BAC at test	Hangover Measure	Control	Measure(s)	Tasks	n	Result	Comment
Anderson & Dawson, 1999	N	B	>1g/kg	-	-	N-A	Attention, Information processing	Symbol digit modalities test, PASAT, Cancellation tests	16 in each	Impaired sustained attention (cancellation tasks) and divided attention (PASAT)	
Bowden et al. 1988	E	-	-	-	-	-	Switching, Fluid Reasoning, Crystallised knowledge	WCST, Shipley Institute of Living Scale		No correlation between performance and drinking	No control, last drinking day average 2.6 days prior to examination = not hangover.
Carroll, Ashe & Roberts, 1964	E	W	105ml absolute alcohol	-	Comment on symptoms	P	Aircraft piloting simulation	Combined motor and visual task simulating skills an aircraft pilot might perform	6	No Effect	
Chait & Perry, 1994	E	W	0.6g/kg males, 0.5g/kg females BAC 0.09%	<0.01 %	-	A+T, A+P, P+T, or P+P	WM, divided attention, STM	DSST, backward Digit span, Logical reasoning, divided attention, free recall	14	No Effect	Unlikely participants were experiencing a hangover (fatigue only as measured by POMS).
Collins 1980	E	W	1.3 g/kg BAC 0.91%	<0.01 %	Hangover Questions	P	Attention	Tracking/RT	8	No Effect	Confounding factor - nicotine consumption

Collins & Chiles, 1978	E	W	1.3 g/kg BAC 0.093%	0.007	Hangover Questions	P	Attention, Psychomotor, Memory & Problem Solving	Choice RT, Pattern Comparison, Problem Solving task	11	No Effect	Confounding factor - nicotine consumption
Devenney & Verster, 2019	N	B	13.8 units	-	AHS	N-A	Attention, Executive Functions, Memory	Erikson Flanker, Stroop, Switching, free-recall, spatial, divided attention tasks	H = 35, NH = 34	Stroop, switching, free-recall impaired. Erikson flanker, divided and spatial attention not effected	
Devenney et al. 2019	N	W	15.4 units	-	AHS	N-A	Attention, Executive Functions, Memory, Psychomotor	Erikson Flanker, Stroop, Switching, free-recall, spatial, psychomotor tasks	43	Spatial working memory, free recall, psychomotor speed impaired. Stroop, Erikson Flanker, Switching not effected	
Dowd, Wolfe, & Cramer, 1973	E	W	0.67 - 1.34 g/kg	24.58 mg%	-	N-A	Aircraft pilloting simulation	Spatial Orientation Trainer	8	No Effect	Alcohol received depended on existing drinking habits. Range of BAC at testing was 0 - 61mg%
Finnigan et al. 1998	E	W	0.7 g/kg	0 except one at 4mg/100ml	Subjective Feelings	P	Attention & Memory	Memory Recall, Tracking/RT, Vigilance	40	No Effect	Main effect of arousal for test day only, when Ps completed Placebo then alcohol

Finnigan et al. 2005	N	B	-	H = 0, AH = 0.002 - 0.124 %	Subjective Feelings, Drug Effects Questions	R-A and N-A	Memory & Attention	Vigilance, Tracking/RT, Memory Recall	H = 25, AH = 13 C = 33	No Effect	Acute Hangover = >1mg/100ml
Gallagher et al. (a) 2011	P-N	B	16.5 units	-	-	N-A	Surgical Performance	MIST-VR	8 in each	Impaired surgical performance	Participants = students
Gallagher et al. (b) 2011	P-N	W	-	0, except 1 >1.0mg/mL	-	N-A	Surgical Performance	MIST-VR	6	Less efficient, more errors at 1pm only	Participants = experts
Grange et al. 2018	N	W	13.6 units eBAC 0.18%	0	AHS	N-A	Psychomotor	Choice RT	31	Psychomotor impaired, information processing slower, more cautious responses	
Hartung et al. 2015	P-N	W	1.34 g/kg	-	-	N-A	Cycling	Cycle around a course	70	Impaired cycling	70 Ps in total, one group of 'residual alcohol' (0.001 – 0.079% BAC)
Heffernan, 2018	N	B	-	0	AHS	N-A	Prospective Memory	PRVP	H = 25, NH = 33	Impaired prospective memory	
Heffernan et al. 2019	N	B	-	0 (or close to 0)	AHS	N-A	Prospective Memory, Executive Functions	Prospective Memory Task, Semantic Verbal Fluency task	H = 19, NH = 22	Impaired Prospective Memory and Semantic Fluency	

Howland et al. 2010	E	W	males = 1.068g/kg females = 0.915 g/kg BAC 0.12%	<0.00 g%	AHS	P	Memory, Academic Performance, Attention	Quiz, GRE & NES-3	193	Visuospatial & Attention/RT impaired. Academic Performance & Memory no effect	
Howse et al. 2018	N	B	H = 10.6 units, NH = 2.66 units	-	mAHSS	N-A	Learning and reward processing	Two-armed bandit gambling task with EEG	H = 30, NH = 28	Reduced performance, reduced reward positivity	Units converted from standard drinks
Idestrom & Cadenius, 1968	E	W	0.8g/kg	0 in blood, traces in urine	-	P	Psychomotor, Motor, Sustained Attention, Visual Perception	Choice RT, TAP, COORD,CFF, Standing steadiness test, Cancellation test	7	No Effect	Mood was measured ("feeling animated, drowsy, tired, happy, depressed, calm, irritated, concentrated") = more tired
Kim et al. 2003	E	W	1.5g/kg (0.075%)	< 0.007	Subjective Hangover Scale	N-A	LNNB	LNNB	13	Visual, Memory, & Intellectual process impaired	
Kocher et al. 2006	P-N	W	10.33 units BAC 0.09%	0	-	N-A	Surgical Performance	Laproscopic surgerical simulator	5	Impaired performance	
Kruisselbrink et al. 2006	E	W	0, 3.41, 6.82, or 10.23 units beer BAC 0.106%	0	Rated Symptoms	N-A	Psychomotor	Choice RT	12	No Effect on Reaction Time, Increased Errors	Female only participants. Units calculated based on reported alcohol consumption

Laurell & Tornros, 1983	P-N	W	1.38 g/kg	0	Severity Ratings	N-A	Driving	Perform avoidance manoeuvre	22	Impaired performance	g/kg calculated from 0.15% BAC
Lemon et al. 1993	E	B	0.5g/kg, 0.75g/kg, 1g/kg BAC 0.083%	0	-	P	Divided Attention, Psychomotor, Vigilance	Rozelle Divided Attention Task, Simple RT, Mackworth Clock	P = 15, Lo = 14, M = 17, Hi = 19	No Effect	Dosages: Low = 0.5g/kg, M = 0.75g/kg, Hi = 1g/kg
McCaul et al. 1991	E	W	1.0 g/kg	-	rated symptoms	P	Memory	Digit Symbol Substitution Test	31	No Effect	Included secobarbital effects in design
McKinney & Coyle, 2004	N	W	males = 14.7 units females = 10.54 units	< 0.01%	Hangover Symptoms Questions	N-A	Memory & Psychomotor	Word Recall & RT	48	Memory & Psychomotor impairments	
McKinney & Coyle, 2007	N	W	males = 16.43 units females = 10.85 units	< 0.01%	Hangover Symptoms Questions	N-A	Memory & Psychomotor	Simple/Choice RT & Word Recall	78	Memory & Psychomotor impairments	Investigated effect of additional stressor (white noise), but had no hangover vs hangover
McKinney et al. 2012	N	W	males = 14.7 units females = 10.54 units	< 0.01%	Hangover Symptoms Questions	N-A	Attention	Erikson Flanker, Stroop, sustained, spatial, divided attention tasks	48	Sustained, Delayed & stroop impaired. Selective attention slowed. Spatial attention not effected	

Morrow, Leirer, & Yesavage, 1990	E	W	0.94 g/kg BAC 0.10%	< 0.001	-	P	Flight simulation	Scenario similar to LOFT, Radio communication		Performance not impaired, more radio communication errors	g/kg calculated from 0.10% BAC
Mrysten et al. 1980	E	W	1.43g/kg	< 0.02%	Hangover severity	A+T or A+P	Psychomotor, Mental Arithmetic, Sustained attention, Spatial memory	Choice RT, Mental arithmetic task, Bourdon test, Coding test, Memory task	12	Impaired; psychomotor speed, arithmetic, coding, and spatial memory	Study on hangover relief - no hangover only condition (hangover + placebo)
Myrsten et al. 1970	E	W	1.13 g/kg	0.004	Hangover Ratings	N-A	Psychomotor, Intellectual ability, Attention	Simple/Choice RT, F-test, & Correction test	15	No Effect	Confounding factor - nicotine consumption. g/kg calculated from 0.12% BAC
Opitz et al. 2019	E	W	0.13% achieved	0	mAHSS	N-A	Executive Functions	Simon NoGo	34	No Effect	Simon GoNo is a task measuring response inhibition
Petros et al. 2003	E	B	1.57 g/kg, 2.36 g/kg BAC 0.112%	-	-	P	Flight simulation	Flight	P = 11, Lo = 13, Hi = 12	3ml/kg dose made more errors for rate of turn and greater deviation from optimal bank position	‘Low’ dose = 1.57g/kg, High dose = 2.36g/kg
Rohers et al. 1991	E	W	0.80g/kg BAC 0.06%	0	Hangover Ratings	P	Attention	Tracking/RT	5	More tracking errors in divided attention task	

Rohsenow et al. 2006	E	W	males = 1.2g/kg females = 1.0g/kg (0.09 - 0.17%)	<0.01 %	AHS	P	Simulated ship performance	Simulation	61	No Effect	
Rohsenow et al. 2010	E	W	males = 1.2g/kg females = 1.1g/kg BAC 0.11%	<0.01	AHS	P	Attention	NES-3	90-91	Sustained attention impaired	
Sepala et al. 1976	E	B	1.75g/kg	12-14 mmol/l	Severity Ratings	T or N-A	Psychomotor, Divided attention	Choice RT, Divided attention task	H = 10, G = 10, Fr = 10, C = 10	Decreased psychomotor accuracy	12mmol/l = 0.055%
Stock et al. 2017	E	W	1.13 g/kg BAC 0.10%	0	-	N-A	Perceptual Decision Making + EEG	Random Moving Dots	19	Larger N2 related to ACC and shorter N2 latency No behavioural effects	g/kg calculated from 0.12% BAC
Streufert et al. 1995	E	W	1g/kg (0.09 - 0.11%)	0	Symptom Questions	P	Managerial Performance	Simulation	21	No Effect	
Tornros & Laurell, 1991	P-N	W	1.66 g/kg BAC 0.176%	< 0.02%	Severity Ratings	N-A	Driving simulation	Complete 20km course as quick as possible	24	No Effect	Impairment at 9:00, but still intoxicated (> 0.02%). 11:30, 14:00, 16:30 were < 0.02%. g/kg calculated from 0.176% BAC

Van Dyken et al. 2013	N	W	0.076 mg/100 mL	0	-	N-A	Simulation	Surgical Performance	27	Decreased accuracy	
Verster et al. 2003	E	W	1.4g/kg BAC 0.155%	0	Reported symptoms and scored	P	Memory & Attention	Word Recall & Macworth Clock	48	Delayed Memory impaired	
Verster et al. 2014	N	W	M = 13.9 units F = 11.3 units BAC 0.133%	< 0.02%	AHS, AHSS, 1-item scale	N-A	Driving	Simulation	42	Driving impairments	4 Ps >0.02% BAC, sensitivity analysis showed no effect. Units converted from standard drinks
Wolff et al. 2016	E	W	1,13 g/kg BAC 0.117%	0	-	N-A	Switching + EEG	Cue- and Memory- based Switching task	23	No effect on Switchin, Lower P3 amplitude	g/kg calculated from 0.12% BAC
Yesavage & Leirer, 1986	E	W	1g/kg	0	-	N-A	Flight simulation	P-3C simulator	10	Impaired pilot performance	
Yesavage et al. 1994	E	W	0.94 g/kg BAC 0.10%	-	-	P	Flight simulation	Frasca 141 Simulator	27	Impaired overall performance	g/kg calculated from 0.10% BAC
Zink et al. 2016	E	W	BAC 0.11%	0	mAHSS	N-A	Executive Functions	Erikson Flanker	20	No Effect	

Note. E = Experimental, N = Naturalistic, P-N = Pseudo-Naturalistic, W = within-subjects, B = between-subjects, A = Alcohol, P = Placebo, T = Treatment, N-A = No-Alcohol, R-A = Residual-Alcohol, LNNB = Luria-Nebraska Neuropsychological Battery, RT = Reaction Time, PASAT = Paced Auditory Serial Addition Task, WCST = Wisconsin Card Sorting Task, WM = Working Memory, STM = Short-term Memory, LTM = Long-term Memory, H = Hangover, AH = Acute &

Hangover, C = Control, NH = No-Hangover, P = Placebo, Lo = Low dose, Mi = Middle dose, Hi = High dose, G = glucose, Fr = Fructose AHS = Acute Hangover Scale, AHSS = Alcohol Hangover Severity Scale, mAHSS = modified Alcohol Hangover Severity Scale, MIST-VR = Minimally Invasive Surgery Trainer-Virtual Reality, PRVP = Prospective Memory Video Procedure, EEG = Electroencephalogram, CFF = Critical Fusion Frequency task, COORD = Coordination test, TAP = Tapping speed task, LOFT = Line-Oriented Flight Training, ACC = Anterior Cingulate Cortex.

1.4 The Current Research

1.4.1 A Systematic Review and Meta-Analysis of the Next-Day Effects of Alcohol Consumption on Cognitive Performance

To address the first aim of this thesis and provide clarity to the hangover literature, Chapter Three will present a systematic review and meta-analysis of the previous hangover literature based on criteria developed in Chapter Two. This criteria will address some of the limitations of previous research (e.g., sensitive outcome measures, appropriate sample sizes) that can also be applied to future experimental studies.

1.4.2 Response Inhibition and Attentional Bias Toward Alcohol-Related Stimuli

The experimental work in Chapter Five will aim to understand how alcohol hangover influences response inhibition and attentional bias toward alcohol-related stimuli, two cognitive processes thought to contribute toward the development of alcohol use disorder (M. Field, Wiers, Christiansen, Fillmore, & Verster, 2010; Goldstein & Volkow, 2002; Jentsch & Taylor, 1999). Alcohol use disorder has been linked to hangover whilst controlling for previous alcohol consumption (Courtney, Worley, Castro, & Tapert, 2018; Piasecki, Robertson, & Epler, 2010); however, the mechanisms involved in this relationship are currently unclear.

It has been theorised that the preferential processing (i.e., attentional bias) of alcohol-related stimuli and poor inhibitory control contribute towards future alcohol-seeking behaviours (M. Field et al., 2010; Goldstein & Volkow, 2002; Jentsch & Taylor, 1999). Models of addiction refer to the development of alcohol use disorder in terms of impaired executive functions, enhanced salience to alcohol or alcohol-related stimuli, and negative affect (Koob, 2013). Studies have previously indicated lower mood during hangover (McKinney, 2010); however, to our knowledge few studies have examined attentional bias and response inhibition during hangover. As highlighted in section 1.4.1, interference control (a form of inhibitory control (Friedman & Miyake, 2004) is impaired by hangover (Devenney et al., 2019; Devenney & Verster, 2019;

McKinney, Coyle, Penning, et al., 2012). However, one experimental study has indicated that response inhibition is unaffected by hangover (Opitz et al., 2019). Experimental designs often administer lower doses of alcohol than are observed in real-life drinking (Verster, de Klerk, et al., 2014) and alcohol consumption is positively related to the cognitive effects of hangover (Rohsenow et al., 2010; Scholey, Benson, et al., 2019b). Therefore, the discrepancy in findings may be due to variations in methodological design and there is a need to investigate the effects of hangover on response inhibition in a study that utilises a naturalistic design.

In relation to attentional processing of alcohol-related stimuli, it is possible that individuals find alcohol aversive during a hangover. Animal studies lend support to this notion. Gauvin et al. (1997) trained rats to drink alcohol freely before injecting them with a high dose of alcohol. During the 'acute withdrawal stage', reflective of a hangover, consumption of alcohol decreased, suggesting an avoidance. However, avoidance of alcohol may be influenced by drinking status as 25% of students who experience a hangover have reported using alcohol as a 'cure' (Hunt-Carter, Slutske, & Piasecki, 2005). These individuals reported higher levels of alcohol consumption and were more likely to meet criteria for AUD symptoms. Together, these results imply that attentional bias towards alcohol-related stimuli may be influenced by hangover, and the extent of attentional bias may be related to drinking status.

Therefore, the first aim of this thesis, the experimental work presented in Chapter Five will investigate the effect of hangover on response inhibition and attentional bias towards alcohol-related stimuli.

1.4.3 Emotion Regulation

Another aim of this thesis is to investigate the effects of alcohol hangover on emotion regulation. Studies have indicated that individuals experiencing a hangover report increased anxiety (Collins & Chiles, 1978; McKinney & Coyle, 2006), lower 'alertness' (greater tiredness; (McKinney & Coyle, 2006; Verster et al., 2003), lower 'tranquillity' ratings (reflective of negative affect, e.g., 'sadness';

(McKinney & Coyle, 2006) and decreased overall mood (Howland et al., 2010). However, the cognitive mechanisms that contribute toward negative affect whilst experiencing a hangover are unclear. One possible mechanism that is utilised to maintain emotional equilibrium is emotion regulation.

Successful emotion regulation decreases negative emotions and physiological activation (Gross, 1998a; McRae et al., 2010), and is essential for managing performance in everyday activities (Gross, Richards, & John, 2006). Emotion regulation is a cognitive process that influences the emotions that an individual experiences, when they occur, and how they are expressed (Gross, 1998a, 1998b, 1999). There are many ways of regulating emotions (Parrott, 1993), but emotion regulation typically uses executive functions and involves allocating resources to the processing and manipulation of information relevant to current emotions (Eysenck et al., 2007). Gross, (1998a, 1998b, 1999, 2015) highlights that emotions can be regulated in a variety of ways such as selecting or modifying a situation (e.g., by avoiding conflict situations), modifying attention (e.g., distraction), modifying responses (e.g., suppression), or changing cognition (e.g., cognitive reappraisal).

Emotion regulation is effortful (Urry, van Reekum, Johnstone, & Davidson, 2009), utilises cognitive resource in working memory (Eysenck et al., 2007; Schmeichel, Volokhov, & Demaree, 2008), and relies on executive functions such as inhibitory control (Joormann, 2010). However, individuals experiencing a hangover have lower energetics (e.g., arousal, effort), indicating that they may be unlikely to engage effectively in effortful cognition (section 1.2.1). Some studies investigating the cognitive effects of hangover have indicated poorer performance on working memory tasks (Howland et al., 2010), whilst other studies indicate that individuals experiencing a hangover have fewer available resources (Scholey, Ayre, Terpstra, & Benson, 2019; Wolff et al., 2016). Further, studies have indicated that aspects of inhibitory control are impaired whilst experiencing a hangover (Benson et al., 2018; Devenney & Verster, 2019; McKinney, Coyle, Penning, et al., 2012). Together these results suggest that emotion regulation processes may be impaired when experiencing a

hangover compared to the morning after no alcohol consumption. To our knowledge, no studies have investigated the effects of hangover on emotion regulation. Therefore, the experimental work presented in Chapter Six aimed to address this gap in the literature.

1.4.4 The Effects of Hangover on Core Aspects of Executive Functions

The final aim of this thesis is to investigate the effects of alcohol hangover on executive function processes. To achieve this aim, it is first important to understand the nature of executive functions. The unity/diversity model conceptualises executive functions in terms of two diverse components and a common factor that underlies all tasks of executive functions (Friedman & Miyake, 2017; Miyake & Friedman, 2012; Miyake et al., 2000). The two diverse factors consist of switching, the ability the divert attention from one task or mental set to another, and updating, the ability to monitor and add/delete information within working memory (Miyake & Friedman, 2012). There has been debate regarding the nature of the common factor, with some arguing inhibition is a key and common factor of executive functions (e.g., Hall & Fong, 2015; Valian, 2015), whilst others propose the commonality reflects fluid general intelligence (e.g., Duncan et al., 1995; Salthouse, 2005). However, Friedman et al. (2006) found the common factor is broader than general intelligence and represents more than Inhibition. Instead, the common factor is thought to reflect the ability to maintain and manage goals (Friedman & Miyake, 2017; Friedman et al., 2008; Gustavson, Miyake, Hewitt, & Friedman, 2015; Miyake & Friedman, 2012). Thus, to investigate the effects of alcohol hangover on core components of executive functions, the study presented in Chapter Seven will investigate how hangover influences an individual's ability to switch, update information, and maintain goals.

As highlighted in section 1.2, factors associated with hangover may influence an individual's ability to switch, update information or maintain goals. Fatigue is one of the most common symptoms of a hangover (Penning et al., 2012a) and can induce impairments in switching (Linden et al., 2003). Furthermore, imbalances in GABAergic and glutamatergic neurotransmission during

hangover could also influence switching (Stock & Beste, 2014). However, a recent study investigating the effect of hangover on performance during an attentional switching task indicated no evidence of hangover-related effects (Wolff et al., 2016). It is possible that results of this study were influenced by the design. Participants were given a set dose of alcohol (achieved BAC 0.12%) in an experimental design, but naturalistic designs (where participants are free to drink the amount and type of alcohol they usually would) often observe greater levels of alcohol consumption (e.g. 0.18%; Grange et al., 2016; Hogewoning et al., 2016). The level of alcohol consumption is positively correlated with the likelihood of experiencing a hangover (Howland, Rohsenow, Allensworth-Davies, et al., 2008; Verster, de Klerk, et al., 2014) and hangover severity (Scholey, Benson, et al., 2019b; Stephens et al., 2017). Furthermore, the strongest predictor of hangover severity is the increased amount of alcohol relative to an individual's normal drinking (Verster et al., 2020). Therefore, it is possible that alcohol consumption in these studies was insufficient to produce a hangover and hangover-related effects (see Chapter Two for further details); however, this is not clear in (Wolff et al., 2016) as hangover severity was not measured.

To our knowledge, no studies have examined the cognitive effects of alcohol hangover on updating or goal maintenance; however, there are indications these processes would be influenced by hangover. Pain (e.g., headache) has an interfering effect on the ability to update information in working memory (Moore, Keogh, & Eccleston, 2013). Furthermore, sleep deprivation (which produces states of high fatigue) can also impair updating abilities (Martínez-Cancino, Azpiroz-Leehan, & Jiménez-Angeles, 2015). As headache and fatigue are 'core' hangover symptoms (van Schrojenstein Lantman, van de Loo, et al., 2017), and individuals often sacrifice sleep time for drinking time (Verster, 2008), it is possible that the ability to update information in working memory becomes impaired during a hangover. For goal maintenance, studies of interference control in hangover may indicate an influence of hangover on goal maintenance. Interference control is the ability to inhibit distractors interfering with on-going cognitive processes and is a component of inhibition needed to maintain goals (Friedman & Miyake, 2004, 2017). Individuals experiencing a

hangover have poorer interference control compared to when not experiencing a hangover (Benson et al., 2018; Devenney & Verster, 2019; McKinney, Coyle, Penning, et al., 2012). As interference control is important for goal maintenance, these studies suggest hangover may also negatively impact an individual's ability to maintain goals. Furthermore, recent studies have found hangover-related impairments in a variety of tasks utilising executive functions; including prospective memory (Heffernan, 2018; Heffernan et al., 2019), verbal semantic memory (Heffernan et al., 2019), spatial working memory (Devenney et al., 2019), and reward learning (Howse et al., 2018). It is therefore possible that goal-maintenance, being the common factor for all tasks of executive functions, is impaired during hangover.

In summary, core executive functions are comprised of two diverse factors (switching and updating) and one unitary factor (goal maintenance). Several factors of a hangover, including symptoms such as headache and fatigue, sleep deprivation, and psychopharmacological alterations, suggest switching, updating, and goal maintenance may be impaired the morning after a night of heavy drinking.

1.5 Conclusion

The overall aim of this thesis is to explore the cognitive effects of alcohol hangover. Currently, research investigating the cognitive effects of hangover has produced mixed results that prevent firm conclusions, thus there is a need for greater clarity. Recently, research has indicated that behaviours utilising executive functions are impaired in hangover, but few studies have investigated the effect of hangover on cognitions that contribute to future alcohol consumption. Furthermore, few studies have investigated the effects of hangover on emotion regulation or the effects of hangover on core components of executive functions (switching, updating, and goal-maintenance). Therefore, this thesis has four aims: 1) To provide clarity to the research literature by conducting a systematic review and meta-analysis of research (Chapter Three), 2) To investigate the effects of alcohol hangover on response inhibition and attentional bias towards alcohol-related stimuli, i.e., cognitive processes

involved in future alcohol consumption (Chapter Five), 3) To investigate the effects of alcohol hangover on emotions and emotion regulation (Chapter Six), and 4) To investigate the effects of alcohol hangover on the core components of executive functions; switching, updating, and goal-maintenance (Chapter Seven).

Before these aims are addressed, it is first important to understand how the variation in the methodological approaches used in the literature may have contributed to the mixed findings that have been reported, and to develop a rigorous methodology that can be utilised in the subsequent studies of this thesis. The following chapter will discuss these points in detail.

Chapter Two: Methodological Approaches and their Contribution to Inconsistent Results

2.1 Introduction

As suggested in Chapter one, limitations in methodology often contribute to inconsistent findings regarding the cognitive effects of alcohol hangover. Several reviews have highlighted the variety in methodology adopted by hangover research and limitations that may contribute to inconsistent results (Prat et al., 2008; Stephens et al., 2014, 2008). These limitations have included variability in defining alcohol hangover, differing methodological designs (e.g., naturalistic alcohol consumption versus experimental administration), and poor methodological rigour (e.g., small sample sizes). To address these concerns, researchers came together at a satellite meeting of the Research Society on Alcoholism conference in 2010 to develop a statement on best practice in alcohol hangover research (Verster et al., 2010). The Alcohol Hangover Research Group (AHRG) consensus statement included methodological guidelines that built on the work of previous authors, and identified pitfalls in earlier research. The authors highlighted several points of consideration for hangover research, including; research design, dose of alcohol consumed, blood alcohol concentration (BAC) at testing, measurement of hangover, and choice of cognitive tests. In the years since this statement, there have been further developments in the methodology used in hangover research. This chapter will discuss limitations of previous methodological designs and how these may have contributed to inconsistent findings in the hangover literature. This chapter will also outline how the experimental studies in this thesis will address these limitations.

2.2 Definition

Differences in definitions of a hangover may contribute to the variety of methodologies that have been adopted in previous research (Prat et al., 2008). Having a clear definition of an alcohol hangover is important, not only for conceptual clarity, but also for considering methodological approaches when investigating hangover effects. Definitions of alcohol hangover have generally contained three elements; i) identification of experiencing a hangover (e.g.,

symptoms), ii) the amount of alcohol consumed that leads to experiencing a hangover, and iii) BAC at the onset of a hangover. Most researchers agree that alcohol hangover can be recognised by negative physiological symptoms, such as headache and nausea, and often describe it as a condition of 'general misery' (Grange et al., 2016; Hogewoning et al., 2016; Prat et al., 2009; Slutske, Piasecki, Nathanson, Statham, & Martin, 2014). Other researchers have differentiated the types of symptoms that can be experienced during an alcohol hangover, recognising that there are also cognitive (Karadayian et al., 2015; Penning et al., 2013, 2012a; Verster, 2008; Verster et al., 2010) and emotional (Huntley et al., 2015; Verster, 2008) effects that can influence everyday behaviours (Penning et al., 2013, 2012a). Despite the amount of alcohol consumed being important to the experience of a hangover, some researchers have omitted details of alcohol consumption from their definitions of hangover (Courtney et al., 2018; Grange et al., 2016; Hogewoning et al., 2016; Rohsenow, Howland, Minsky, & Arnedt, 2006; Verster, 2008, 2009; Verster et al., 2010). As will be discussed in detail later (section 2.3), studies suggest that lower doses of alcohol may be unlikely to result in the experience of hangover. For example, a survey investigating naturalistic drinking behaviours reported that more than half of participants (53.8%) said they did not experience a hangover after a drinking episode with a BAC of 0.08% (Verster, de Klerk, et al., 2014). Furthermore, a recent consensus paper suggests that it is the increase in alcohol consumption during a heavy drinking episode relative to normal alcohol consumption that is important in predicting hangover severity (Verster et al., 2020).

There has also been disagreement surrounding the onset of an alcohol hangover. Specifically, if cognitive tests should begin when alcohol is still present in the body (typically measured by exhaled breath alcohol concentration of participants or via blood sampling). Some researchers specify that BAC should be zero (Grange et al., 2016; Prat et al., 2009; Verster, 2008), whilst others state hangovers occur when BAC is *approaching* zero, but that low residual levels can be present (Huntley et al., 2015; Slutske et al., 2014). These different perspectives could dramatically alter how studies are conducted and influence results. For example, one approach to ensure that BAC is zero when

participants complete cognitive and subjective measures is to delay start time (Rohsenow et al., 2010). However, as peak hangover symptoms occur 12 – 14 h after alcohol consumption (Ylikahri et al., 1974), symptoms and potential hangover-related effects may begin to subside during this delay. In contrast, studies in which BAC is approaching zero may be able to test participants at peak hangover severity, but risk interference of acute intoxication effects. To further complicate matters, a BAC of zero assessed by breathalyser does not assure ethanol is eliminated entirely from the blood (Verster, Mackus, Van de Loo, Garssen, & Scholey, 2017).

In a recent attempt to provide some conceptual clarity, a definition for alcohol hangover was developed using consumer descriptions and academic consensus (van Schrojenstein Lantman, van de Loo, et al., 2017). The authors asked students who had recently experienced a hangover (n = 1099) to give their best definition of an alcohol hangover and to list the hangover symptoms they experience. The authors highlighted four 'core' symptoms of hangover (nausea, headache, being tired, apathy), constructed three potential definitions, and then presented these to members of the AHRG for expert opinion. Expert consensus (n = 16) from various research groups around the world was reached for the definition "The alcohol hangover refers to the combination of mental and physical symptoms, experienced the day after a single episode of heavy drinking, starting when BAC approaches zero" (Van Schrojenstein Lantman et al., 2017, pp. 153). The new definition, which this thesis will adopt, recognises that a hangover involves the experience of a variety of symptoms (e.g., headache, fatigue, stomach ache etc.). It also recognises that the amount of alcohol consumed is an important factor, and that BAC does not have to be zero (i.e. *approaches* zero). This definition is not without limitations as defining a hangover based on symptoms negates the processes that underlie the emergence of the symptoms. Hangover symptoms are a result of a causal process – i.e., the body returning to normal physiological functioning in response to a toxin (alcohol). However, it is not currently possible to define hangover through underlying biological mechanisms as they are currently unknown. Furthermore, the term 'heavy' alcohol consumption is vague, but was agreed upon to reflect individual variability in the amount of alcohol consumed

prior to the experience of a hangover. To summarise, this thesis will adopt this new definition to investigate the cognitive effects of alcohol hangover, and use it as a guide to address limitations in previous methodological approaches.

2.3 Design

Hangover has traditionally been studied using two distinct approaches; experimentally-induced hangover, or naturalistic hangover. The experimental approach emulates the 'gold-standard' randomised control trials for psychopharmacological research by including double-blind, placebo-controlled procedures. A within-subject design is often used to account for individual variability in terms of the effects of alcohol (Martin & Sayette, 1993). Participants are given alcohol (usually vodka and orange), and placebo (orange juice with a small amount of vodka 'floated' on top for smell) in a fixed (often short) period and in a randomised, counterbalanced order. The researcher administering drinks and the participant are unaware of the order of consumption and condition until the end of the study. This double-blind manipulation helps to prevent influence from expectations about alcohol consumption, such as the participant and researcher expecting impairments due to hangover. The amount of alcohol administered is controlled so that participants reach a similar BAC, usually conducted by administering a set g/kg of alcohol according to body weight. However, in hangover research there is a trend toward administering alcohol at a set BAC% (e.g., 0.12%; Howland et al., 2010; Rohsenow et al., 2010). This is accomplished by first administering a set g/kg of alcohol, and then when measuring BAC (e.g., with a breathalyser), 'topping up' participants until they reach the desired peak BAC. Researchers administer alcohol in an evening and participants complete cognitive tasks in the laboratory the following morning, where extraneous variables (e.g., noise) can be controlled for to prevent their influence on performance. Participants usually receive the dose of alcohol in an evening, often with a standardised meal, and either go home to return the next morning or sleep in the laboratory if facilities are available. Testing then typically begins when participant's BAC returns to zero.

An alternative approach to experimentally-induced hangover, is to study participants after a night of naturalistic alcohol consumption – i.e., the naturalistic approach. Researchers ask participants to attend cognitive testing in the laboratory on a morning when they are likely to be experiencing a hangover. Participants are free to drink the amount of alcohol and type of beverage that they usually would, and no controls are set around drinking time or location. This approach reflects real-life alcohol consumption and subsequent hangovers, which increases the ecological validity of studies. Both the experimental and the naturalistic approaches are considered to have merit and are often discussed together (Verster et al., 2010). However, differences between study designs may be a factor that has contributed to mixed findings in the hangover literature.

The approach adopted may influence the likelihood of observing hangover-related effects. For example, studies that have explored psychomotor speed using simple reaction times (responding to a single stimulus) or choice RT (e.g., responding when one of five lights turn on) tend to report impairments when a naturalistic design is adopted (Devenney et al., 2019; Grange et al., 2016; McKinney & Coyle, 2004, 2007) but not when an experimental design is used (Collins, 1980; Collins & Chiles, 1978; Kruisselbrink et al., 2006; Lemon et al., 1993; Myrsten et al., 1970), although Kruisselbrink et al., (2006) reported decreased accuracy during the hangover condition. The inconsistent findings between the experimental and naturalistic approach may be due to factors associated with alcohol consumption that are different between the two approaches. As highlighted by Finnigan and Hammersley (1992, as cited in Stephens, Grange, Jones, & Owen, 2014), the amount of alcohol consumed and type of drink could influence the effects of alcohol.

Although the naturalistic approach may lack control over certain aspects of alcohol consumption (type of drink, time drinking, amount of alcohol), it offers an ecologically valid design that captures hangover effects following an episode of heavy drinking (Verster et al., 2019). The amount of alcohol consumed has been linked to hangover frequency (Penning et al., 2012a) and severity (Scholey, Benson, et al., 2019b; Stephens et al., 2017). These are important

factors to consider when designing hangover studies in order to maximise the likelihood of participants experiencing a hangover within the hangover condition (Verster et al., 2019). Furthermore, hangover severity is negatively associated with cognitive performance during a hangover (Scholey, Benson, et al., 2019b), suggesting that the cognitive effects of a hangover are most likely observed following higher amounts of alcohol consumption. Figure 2.1 shows that the experimental design typically administers lower doses of alcohol than the alcohol consumed in naturalistic designs ((e)BAC 0.10% and 0.14% respectively). This is important, particularly as both experimental and naturalistic studies include samples from populations with similar level of alcohol consumption (e.g., students). A recent consensus paper of the AHRG suggest that the increase in alcohol consumption during a heavy drinking episode relative to normal drinking is an important predictor of hangover severity (Verster et al., 2020). As the naturalistic approach includes greater levels of alcohol consumption it may be the most appropriate to use when investigating the cognitive effects of alcohol hangover as participants are more likely to consume significantly more alcohol than normal.

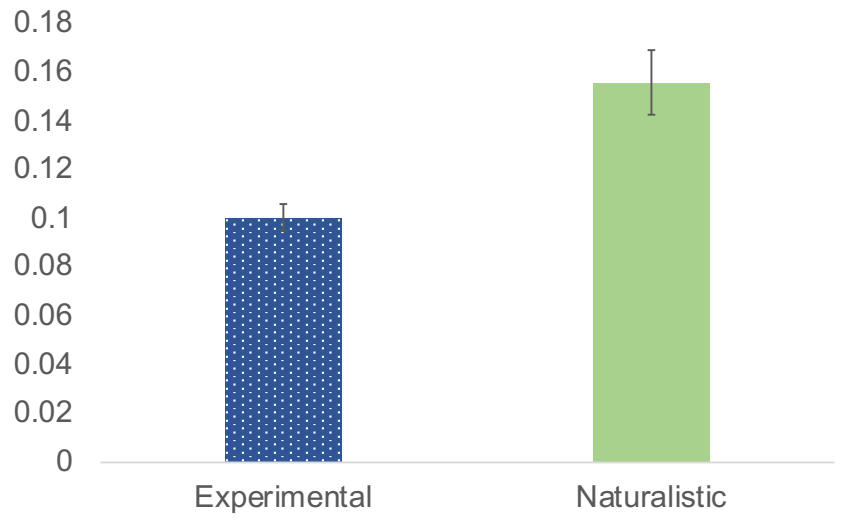

Figure 2.1. Mean (e)BAC for the studies presented in Table 1.2 that utilise the experimental or naturalistic approach and report BAC or eBAC. For experimental studies, mean (SD) BAC was 0.10% (0.02), and for naturalistic studies mean (SD) eBAC was 0.16% (0.04). (e)BAC, (estimated) Blood Alcohol Concentration. Error bars represent ± 1 Standard Error of the Mean.

Some hangover researchers have suggested that congeners, by-products of the alcohol fermentation process (e.g., methanol), may be important to the experience of a hangover (Caldar, 1997; Damrau & Liddy, 1960; Rohsenow et al., 2010). As it is not practically feasible to control alcohol consumption with the naturalistic approach, congeners are a potential confound in this design. However, although Rohsenow et al. (2010) reported higher hangover severity following whisky compared to vodka drinking, congener content did not influence cognitive performance. Therefore, the extent to which congeners influence cognitive performance during is unclear, and as controlling congener content is not feasible within a naturalistic design, this issue shall not be considered further.

To conclude, although both approaches to studying alcohol hangover are seen to have merit, the naturalistic design offers an ecologically valid insight into the effects of alcohol hangover. Relative to the experimental approach, higher amounts of alcohol consumption are observed with naturalistic designs, which in turn could influence the likelihood of participants experiencing hangover, the intensity of hangover experienced, and cognitive effects reflective of real-life hangovers. Therefore, studies in this thesis will adopt a naturalistic design toward investigating the cognitive effects of alcohol hangover. However, methodological rigour in previous hangover studies has typically been low. Below we shall discuss previous limitations of studies and develop a rigorous methodology that can be taken forward for the studies described in Chapters Five, Six and Seven of this thesis.

2.4 Participants

2.4.1 Sample Size

A major concern in hangover research has been low statistical power due to small sample size. As highlighted by the AHRG, alcohol hangover studies performed before 1990 typically contain less than 10 participants (Verster et al., 2010). Button et al. (2013) discussed the issue of low power, caused by small sample sizes, indicating that it can severely harm a research field. They highlight that low powered studies have a low chance of discovering effects

and, if they do find an effect, there is a low probability it would reflect a true effect. Even if a true effect were observed, the effect estimate would be exaggerated, which in turn could affect the design and conclusions of future studies. Low powered studies have a greater range of effect estimates, are often of poor design, and likely to be affected by publication bias and selective reporting, which can influence the reliability of the evidence (Button et al., 2013).

An example of how small samples may prevent firm conclusions in the hangover literature can be seen in studies investigating choice RT. Typically, studies with a small sample size (*n*s < 15) report no evidence of hangover-related effects (Collins & Chiles, 1978; Ideström & Cadenius, 1968; Kruisselbrink et al., 2006; Myrsten et al., 1970). However, studies with larger sample sizes (*n*s > 31) indicate that choice RT is impaired by hangover (Grange et al., 2016; McKinney & Coyle, 2004, 2007). As small sample sizes are not unique to studies of choice RT, but are typical for many aspects of cognition in hangover research (Verster et al., 2010), an important step would be to provide greater clarity to the inconsistent findings. One way to provide clarity to this field and address concerns of small sample size would be to conduct a meta-analysis (Button et al., 2013), which examines effect sizes across multiple studies to determine if there is an 'overall' effect. This thesis presents a meta-analysis of the effects of hangover on cognition alongside a systematic review presented in Chapter Three.

The AHRG recommends a-priori sample size power calculations for future research (Verster et al., 2010). However, as the experimental work in this thesis aims to investigate the effects of alcohol hangover on executive functions or cognitions reliant on executive functioning, the paucity of research investigating hangover and executive functions make this difficult. In this case, it would be appropriate to calculate sample sizes based on studies investigating hangover effects of other relevant cognitive domains. For example, to our knowledge there are no studies that investigate the effects of alcohol hangover on emotion regulation (Chapter Six in this thesis), so sample sizes from studies of

interference control (e.g., McKinney et al., 2012) could be used, as inhibition is needed to regulate emotions (Joormann, 2010).

2.4.2 Recruitment

Despite 85% of UK university students engaging in heavy episodic drinking, i.e., exceeding 8 units of alcohol on a single occasion (John & Alwyn, 2014), there are some significant challenges to recruiting participants for hangover research. For example, one study recruited 100 participants to investigate the effects of alcohol hangover on choice RT (Grange et al., 2016). However, their final sample was reduced to n = 31 – an attrition rate of 69%. Reasons for exclusion included; participants attending one session only, positive or missing BAC data at the time of testing, and not drinking before the hangover condition or drinking before the no-hangover condition. Similarly, Howland et al. (2010) reported 196 participants completed their study, despite recruiting 364 eligible participants (attrition of 54%). Individuals acknowledge and anticipate the unpleasant effects of an alcohol hangover, preferring to stay at home and watch movies (Griffin et al., 2018), which could contribute to attrition (e.g., missed scheduled testing sessions). Acknowledging the unpleasant effects of hangovers may also leave potential participants less likely to volunteer for hangover research, which may contribute to issues with small sample sizes in the literature (section 2.4.1). Therefore, the current thesis explores various flexible recruitment strategies, such as the participant harvesting method (Crandall, Schiffhauer, & Harvey, 1997); Chapter Six) and flexibility in terms of testing locations (Chapters Six and Seven), which could enable greater attainment of adequate sample sizes for effects to be observed.

2.4.3 Criteria

Recent research has highlighted that hangover-resistance could be a potential confound in the hangover condition. Hangover-resistance is the absence of hangover symptoms (except a mild increase in drowsiness (Hogewoning et al., 2016)) despite drinking large amounts of alcohol, and may occur in approximately 10% of alcohol drinkers (Kruisselbrink et al., 2017; Verster, de Klerk, et al., 2014). Hangover-resistant individuals do not appear to experience

alcohol intoxication differently to those who experience a hangover (Mackus, van Schrojenstein Lantman, et al., 2018). It is therefore possible that previous null results may be influenced by including participants that experienced fatigue only during the hangover condition (e.g., Finnigan et al., 1998) due to the confound of hangover-resistance. Thus, hangover research should control for hangover-resistance within study designs.

One way to ensure that participants experience hangover symptoms is to adopt criteria that excludes participants who do not report experiencing hangovers (Finnigan, Schulze, Smallwood, & Helander, 2005b). This approach was adopted for experimental studies throughout this thesis alongside criteria to include participants that regularly engage in heavy episodic drinking. These criteria would ensure that participants; i) experience hangovers (and are therefore not hangover-resistant), ii) consume enough alcohol to likely experience a hangover, and iii) are not consuming more than they would typically drink to take part in the study. This approach is also ethically beneficial as it only seeks to recruit participants who regularly drink heavily. Another way to prevent hangover-resistance influencing results, which can be used in conjunction with inclusion criteria, is to include a measure of hangover severity in the study design. The recently agreed upon definition of alcohol hangover highlights that alcohol hangover can be recognised through a variety of symptoms (van Schrojenstein Lantman, van de Loo, et al., 2017), which can, and should, be measured (see section 2.6.1).

2.5 Conditions

2.5.1 Control

The use of adequate control conditions in experimental designs ensure internal validity (Mohr et al., 2009). In hangover research (as with all experimental research) an appropriate control condition is necessary for adequate comparison and determination of treatment effects. However, this has not always been the case. For example, Takala, Siro, and Toivainen (1958) investigated the cognitive effects of hangover by comparing a group of medical students in the hangover condition with a group of psychology and technology

students in the no-hangover condition. As previous reviews of the cognitive effects of alcohol hangover have highlighted (Stephens et al., 2008), comparing intact groups in this way prevents distinguishing from hangover effects and pre-existing participant differences. Since these early studies, there has been much progress in research design and adequate controls are typically used to ensure internal validity. However, debate now focuses on the most appropriate control to use, with some utilising a placebo control (e.g., Rohsenow et al., 2010), whereas others view a no-hangover control as both adequate and the only practical option (e.g., McKinney & Coyle, 2004).

A valid criticism of using the naturalistic approach to explore the effects of hangover on cognition is the lack of placebo control. As the hangover condition follows a night of heavy drinking that the participant planned themselves, participants are aware of which condition they are in. Some researchers have suggested placebo controls could be adopted in naturalistic studies by arranging testing for days that a researcher thinks it likely participants would be experiencing a hangover (e.g., the morning after a student club night or weekends; (Stephens et al., 2014). However, even studies that have adopted an experimental approach with a placebo control have reported 84% of participants correctly identify conditions (Rohsenow et al., 2010). The effects of high amounts of alcohol necessary to induce a hangover may allow participants to identify substances that do not cause this level of intoxication (i.e., the placebo). Indeed, it has previously been highlighted that placebo conditions are ineffective at doses of alcohol above 0.08% (Rohsenow & Marlatt, 1981). Together these data suggest that placebo controls are not effective when either a naturalistic or experimental approach is used to measure the cognitive effects of alcohol hangover.

An alternative to the placebo control is a no-treatment control condition (i.e., participants not consuming alcohol for a period before testing – a no-hangover control). In a meta-analysis that combined data from studies that compared placebo treatments to no-treatment controls, there were no significant overall effects of placebo interventions (Hróbjartsson & Gøtzsche, 2002). No overall

effect of placebo compared to no-treatment has also been observed in a meta-analysis of three-armed trials (no-treatment, placebo, and treatment conditions; (Koog, We, & Min, 2012). Together, these studies suggest that no-treatment controls are adequate for use in hangover research. Research in this thesis will therefore include a no-hangover control condition, which asks participants to attend a testing session following alcohol abstention for at least 24 hours.

2.5.2 Hangover

The AHRG consensus statement of best practice in hangover research argued that the amount of alcohol consumed is an important aspect of the hangover condition (Verster et al., 2010). By adopting a naturalistic design, participants are likely to consume a higher amount of alcohol than typically administered within an experimental approach. Furthermore, by adding the criteria that participants have experienced a hangover within the past month, hangover conditions can control for the potential influence of hangover resistance (section 2.4.3). Despite adopting a naturalistic approach and controlling for hangover-resistance, it is difficult to ensure participants are experiencing a hangover without directly measuring symptoms due to individual variability in the quantities of alcohol consumed before a hangover is experienced (Chapman, 1970; Howland, Rohsenow, Allensworth-Davies, et al., 2008; Verster, de Klerk, et al., 2014). There is also no reliable biochemical verification of hangover available, unlike intoxication, which can use breathalyser to validate alcohol consumption. Therefore, it is also important that studies include a measure of hangover severity to improve the validity this condition.

Another important factor that has contributed toward differences in defining hangover (see section 2.2) and is often debated is the amount of alcohol that remains within the blood at testing. Previously it was argued that testing should begin when BAC is zero (Verster et al., 2010). However, recently this view has been questioned (Verster et al., 2017), particularly as the definition of alcohol hangover highlights hangover occurs when BAC is *approaching* zero (van Schrojenstein Lantman, van de Loo, et al., 2017). Furthermore, recent research has indicated that alcohol is still present in the blood and urine of participants

despite zero Breath Alcohol Concentration (BrAC; Verster et al., 2017). This suggests participants in previous research that conducted cognitive tests when BrAC was zero may have had residual alcohol present. It has therefore been recommended that cognitive testing could begin when BAC is still present, but approaching zero (Verster et al., 2017). Several studies appear to have taken this view by omitting measurement of BAC at testing (Anderson & Dawson, 1999; Hartung et al., 2015; Howse et al., 2018; McCaul et al., 1991; Petros et al., 2003). However acute alcohol intoxication can have cognitive effects at BACs as low as 0.02% (Holloway, 1994), and by not measuring BAC at testing, it is not possible to differentiate between intoxication-related and hangover-related effects.

When included in hangover studies, participants with a BAC > 0.02% could dramatically influence results. For example, acute intoxication studies have shown impaired psychomotor skills related to driving (Christoforou, Karlaftis, & Yannis, 2013). Impaired psychomotor skills related to driving have also been found in a study of alcohol hangover (Seppälå, Leino, Linnoila, Huttunen, & Ylikahri, 1976). However, participants in this study measured a BAC of approximately 0.05% the morning after alcohol consumption, indicating that they were still intoxicated. Therefore, the next-day effects observed by Seppälå et al. (1976) may be confounded by alcohol still circulating in the blood of participants. Furthermore, the differential effect of residual alcohol the morning after a night of heavy drinking and hangover on a simulated driving task, reflective of a short commute to work, has recently been investigated (Alford, Broom, Lands, Johnson, & Verster, 2018). Although participants who experienced a hangover exhibited impaired vehicle control relative to no-hangover, including increased speed and double the number of lane excursions, those who had residual alcohol (BAC > 0.05%) performed poorer than those that had no residual alcohol. Taken together these findings indicate that including individuals with residual alcohol during hangover within study designs may influence results. Therefore, studies in this thesis will set a threshold BAC that limits the likelihood of residual alcohol influencing results (0.02%), or account for residual alcohol in statistical analysis (via sensitivity analysis). It should be noted, in some studies that included participants that had

residual alcohol > 0.02% (e.g., Verster, Bervoets, et al., 2014; *n* of residual alcohol > 0.02% = 4), sensitivity analysis revealed inclusion of these participants did not change results (correspondence with authors).

In summary, a no-hangover control condition (participants abstain from alcohol 24 hours prior to testing) is adequate, and an effective hangover condition which should ensure that participants are experiencing a hangover at the time of testing. Therefore, the experimental work in this thesis will adopt a no-hangover control condition and measure hangover with a hangover severity scale that measures the intensity of several hangover symptoms (see section 2.6.1 below). Although BAC does not have to be zero when cognitive testing begins, it will be measured in the experimental work of this thesis to differentiate between intoxication-related and hangover-related effects.

2.6 Measurement

2.6.1 Hangover

As highlighted in sections 2.4.3 and 2.5.2, including a measure of hangover severity is important to validate the hangover condition. The current lack of understanding regarding the biological underpinning of an alcohol hangover means that objective measures are currently unavailable. It is known that immunological factors (Kim et al., 2003; A Van de Loo et al., 2015), alcohol metabolites (Swift & Davidson, 1998), neurochemical changes (Maki et al., 1998), hypothalamic-pituitary axis stimulation (Linkola et al., 1979), and sympathetic nervous system activation (Kupari, 1983; Myrsten et al., 1970) play a role. However, their precise contribution to hangover symptoms, severity and effects on cognition is unknown. This uncertainty has contributed to defining hangover by symptomology, rather than underlying biological mechanisms (van Schrojenstein Lantman, van de Loo, et al., 2017). Attempts have been made to establish an objective measure of alcohol hangover using ethyl glucuronide (EtG) and ethyl sulphate (EtS) – metabolites of alcohol that are present in the urine during the hangover period (Mackus, Van de Loo, Raasveld, et al., 2017). 5-hydroxytryptophan (Mackus, van de Bogaard, et al., 2018), and methanol (Mackus, Van de Loo, Korte-Bouws, et al., 2017) have also been explored as

an objective measures of alcohol hangover. However, in all these attempts, concentrations do not correlate with self-reported symptom severity, indicating that although they may be present at increased concentrations during hangover, they do not reflect the intensity of symptoms experienced. These potential biomarkers are also present in hangover-resistant individuals (Mackus, van de Bogaard, et al., 2018; Mackus, Van de Loo, Korte-Bouws, et al., 2017; Mackus, Van de Loo, Raasveld, et al., 2017), further implying that their presence does not contribute to the symptomology of a hangover. In sum, there are currently no viable biomarkers of an alcohol hangover; instead, measurement relies on self-report.

Validated self-report measures typically consists of an individual rating severity of commonly experienced symptoms. The Hangover Symptom Scale (HSS; Slutske, Piasecki, & Hunt-carter, 2003) is a 13-item retrospective questionnaire used in surveys that assesses symptoms experienced over the past 12 months. The Alcohol Hangover Severity Scale (AHSS; Penning et al., 2013) and the Acute Hangover Scale (AHS; Rohsenow et al., 2007) were developed for use in an experimental setting and consist of 12- and 9-items respectively. All three of these scales assess individual symptoms of a hangover, but the symptoms that participants rate are different in each scale. For example, the AHS asks participants to rate the severity of ‘headache’, a common hangover symptom, but the AHSS does not. This variability has led researchers to develop a composite 23-item modified Alcohol Hangover Severity Scale (mAHSS) that incorporates all symptoms from the three scales, alongside a 1-item measure for overall hangover severity (Hogewoning et al., 2016; Howse et al., 2018). For laboratory studies of alcohol hangover, when assessing hangover in real-time (i.e., at the point of experience), the mAHSS is best equipped to determine the severity of a wide range of symptoms and thus will be used for studies in this thesis.

2.6.2 Alcohol Consumption

As experimental work will adopt a criteria that only recruits participants who regularly engage in heavy drinking, studies will measure alcohol consumption

the night before testing through self-report measures. Participants will be asked to report alcohol consumption from the previous night using pictorial prompts that are labelled with unit content. This information will then be used to calculate an estimated peak Blood Alcohol Concentration (eBAC) using the Widmark formula (see equation below; (National Highway Traffic Safety Administration, 1994)), which has been used in previous alcohol research (Andersson, Wiréhn, Olvander, Ekman, & Bendtsen, 2009; Kypri, Langley, & Stephenson, 2005). This will help verify that participants have consumed alcohol quantities likely to result in a hangover. The first experimental study will also ask participants to report alcohol consumption for their 'typical' night of heavy drinking during a screening session. This can then be compared to alcohol consumption the night before the hangover condition to verify that alcohol consumption does not differ from typical heavy drinking.

$$eBAC = \left(\frac{0.806\ x\ SD}{TBW\ x\ Wt} - (\beta_{60}\ x\ DP)\right)$$

Where;

0.806 – constant for body water in the blood (80.6%)

SD – standard drink

TBW – total body water, using 0.58 for males and 0.49 for females

B_{60} – metabolism rate, using 0.017

Wt – weight in kg

DP – drinking period in hours

2.6.3 Task Selection

To improve understanding of the specificity of hangover-related effects on cognition and to prevent nebulous findings in hangover research, it has been recommended to include psychological tasks that measure a singular construct. Measures of a singular construct have not always been adopted in hangover

research, instead studies have included general measures that span various cognitive domains (Anderson & Dawson, 1999; Chait & Perry, 1994; Kim et al., 2003; McCaul et al., 1991; Myrsten et al., 1970, 1980; Petros et al., 2003). For example, Kim, Yoon, Lee, Choi, and Go (2003) investigated the cognitive effects of alcohol hangover with the Luria-Nebraska Neurobehavioural Battery (LNNB), which is a screening tool used by clinicians to assess brain injury. Although the authors report significant hangover-related impairments in visual, memory, and intellectual processes compared to baseline (before drinking), the specific cognitive components involved are unclear. The memory component of the LNNB comprises short-term (STM), long-term (LTM), and working memory. As Chapter One highlighted, STM and LTM may be impaired in alcohol hangover, but the impact on working memory is still unclear. Thus it is difficult to determine the effects of alcohol hangover on each component of memory in the LNNB task.

The recommendation to include psychological tasks that measure a singular construct is an important one that should be adopted where possible. However, the main aim of this thesis is to investigate the cognitive effects of alcohol hangover on executive function processes. Tasks designed to measure executive functions are inherently impure as executive functions combine several cognitive processes to complete goals (Husain, 2017; Miyake et al., 2000). For example, a switching task (e.g., Monsell, Sumner, & Waters, 2003) may present a number inside a coloured shape and participants respond according to a rule determined by the colour of a shape (odd/evens or high/low). Completion of this task requires participants to switch between rules effectively, but also requires other cognitions such as visuospatial, numerical, and psychomotor skills. Although tasks may measure multiple cognitive constructs, executive functions are essential for successful performance in everyday behaviours and are thus an important cognitive processes to assess the effects of alcohol hangover (Stephens et al., 2014).

Another important consideration for task selection is one of sensitivity. The AHRG consensus statement advises tasks should be selected that are sensitive

to the effects of alcohol hangover or have a mechanistic connection to hangover (Stephens et al., 2014; Verster et al., 2010). As highlighted in Chapter One, hangover literature is scarce (relative to other alcohol research), particularly studies investigating the effects of hangover on executive function. Tasks of executive function sensitive to the effects of alcohol hangover have therefore not been established, and so the selection of tasks should be based upon a mechanistic connection to hangover or based upon sensitivity to the effects of alcohol in general. For example, the n-back task is a measure of an individual's ability to update information within working memory (Jaeggi, Buschkuehl, Perrig, & Meier, 2010). A 2-back version of the task has previously been used to highlight the detrimental effects of acute intoxication on working memory (Casbon, Curtin, Lang, & Patrick, 2003), and thus would be suitable to study the effects of alcohol hangover on updating (a component of executive functions). Table 2.1 highlights that the cognitive tasks utilised throughout this thesis have previously demonstrated sensitivity to show effects of mechanisms related to alcohol hangover.

Table 2.1. Tasks used in experimental work and justification of sensitivity

Task	Cognition measured	Chapter	Sensitivity	Reference
Go/No-Go	Response inhibition	Chapter Five	Alcohol, sleep loss	Kreusch, Vilenne, & Quertemont, 2013
Visual Dot Probe	Attentional bias towards alcohol-related stimuli	Chapter Five	Alcohol	Adams, Ataya, Attwood, & Munafò, 2012
Emotion regulation task	Cognitive reappraisal	Chapter Six	Anxiety and depression	Goldin, Ball, Werner, Heimberg, & Gross, 2009 Erk et al., 2010
S-DERS	Emotion Dysregulation	Chapter Six	Alcohol	Lavender, Tull, DiLillo, Messman-Moore, & Gratz, 2015
Switching task	Switching	Chapter Seven	Headache	Attridge, Eccleston, Noonan, Wainwright, & Keogh, 2017
n-back	Updating	Chapter Seven	Acute intoxication, Headache	Moore, Keogh, & Eccleston, 2013; Casbon, Curtin, Lang, & Patrick, 2003
AX-CPT	Goal maintenance	Chapter Seven	Alcohol dependence	Rubio et al., 2007

Note. S-DERS, State-Difficulties in Emotion Regulation Scale

2.7 Conclusion

Many factors, such as defining a hangover, study design, participant characteristics, validating hangover experiences, and confounding factors, have contributed toward inconsistent findings in studies investigating the cognitive effects of alcohol hangover. The experimental work reported in this thesis will adopt the recent definition of hangover has academic consensus. This definition will be used to build upon limitations of previous research and improve methodological rigour when investigating the effects of alcohol hangover on executive functions. In order to maximise the validity of the hangover condition and to reflect real-life hangover experiences, experimental work in this thesis will adopt a naturalistic design. Sample sizes will be calculated a-priori to ensure sufficient recruitment to observe an effect, and different recruitment strategies will be explored to minimise participant attrition. Only participants who have experienced a hangover in the past month will be included in the study to control for hangover-resistance, and a hangover sensitivity measure will be used to improve the validity of hangover conditions. To differentiate between intoxication-related and hangover-related effects, BAC will be measured at testing and studies will either conduct testing when BAC < 0.02% (Chapter Five), or conduct sensitivity analysis using BAC 0.02% as a threshold (Chapters Six and Seven). Tasks will also be selected based on previously established sensitivity to alcohol effects or mechanisms underlying hangover. However, before utilising this new methodological approach in experimental work, the following chapter will address the first aim of this thesis, i.e., to provide clarity to the mixed literature. It will do this by systematically review the literature based upon criteria that fits with the rigorous methodology outlined above and by using meta-analytical techniques to estimate the overall effect of alcohol hangover on cognition.

Chapter Three: A Systematic Review of the Next-Day Effects of Alcohol Consumption on Cognitive Performance

Declaration of Authorship

This declaration concerns the article entitled:			
A systematic Review of the Next-Day Effects of Alcohol Consumption on Cognitive Performance			
Publication status (tick one) **Draft manuscript** [ ] **Submitted** [ ] **In review** [ ] **Accepted** [ ] **Published** [X]			
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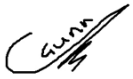
Candidate's contribution to the paper (provide details, and also indicate as a percentage)	The candidate contributed to / considerably contributed to / predominantly executed the… Formulation of ideas: Predominantly executed Design of methodology: Predominantly executed Experimental work: Predominantly executed Presentation of data in journal format: Considerably contributed		
Statement from Candidate	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature.		
Signed		**Date**	13/02/2020

A Systematic Review of the Next-Day Effects of Heavy Alcohol Consumption on Cognitive Performance

Craig Gunn[1], Marlou Mackus[2], Chris Griffin[1], Marcus R. Munafò[3,4], Sally Adams[1]

[1] UK Centre for Tobacco and Alcohol Studies and Department of Psychology, University of Bath.

[2]Utrecht Institute for Pharmaceutical Sciences, Department of Psychopharmacology, Utrecht University, Utrecht, Netherlands

[3] UK Centre for Tobacco and Alcohol Studies and School of Experimental Psychology, University of Bristol, UK.

[4] MRC Integrative Epidemiology Unit (IEU) at the University of Bristol, UK.

Corresponding author: Craig Gunn, Department of Psychology, University of Bath, Bath, BA2 7AY, United Kingdom. F: +44. 1225. 386752; E: c.a.gunn@bath.ac.uk

Preregistered hypothesis:

http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017054617

3.1 Abstract

Aims. Studies examining the next-day cognitive effects of heavy alcohol consumption have produced mixed findings, which may reflect inconsistencies in definitions of 'hangover'. Recent consensus has defined hangover as "mental and physical symptoms, experienced the day after a single episode of heavy drinking, starting when blood alcohol concentration (BAC) approaches zero". In light of this, we aimed to systematically review the literature to critically evaluate and estimate mean effect sizes of the next-day effects of heavy alcohol consumption on cognition. Design. Embase, PubMed and PsycNET databases were searched between December 2016 and May 2018 using terms based on 'alcohol' and 'hangover'. Studies of experimental design which reported the next-day cognitive effects of heavy alcohol consumption in a 'hangover' group with BAC < 0.02% were reviewed. 1163 participants across 19 studies conducted since 1970 were included in the analysis. Measures. Data for study design, hangover severity, BAC at testing, and cognitive performance was extracted and effect estimates calculated. Findings. 805 articles were identified. 39 full-text articles were screened by two independent reviewers and 19 included in the systematic review. 11 articles provided sufficient data to be included in the meta-analysis. The systematic review suggested that sustained attention, and driving abilities were impaired during hangover. Mixed results were observed for: psychomotor skills, short- and long-term memory, and divided attention. The meta-analysis revealed evidence of impairments in STM (g = 0.64, 95% CI 0.15 to 1.13), LTM (g = 0.59, 95% CI 0.01 to 1.17) sustained attention (g = 0.47, 95% CI 0.07 to 0.87), and psychomotor speed (g = 0.66, 95% CI 0.31 to 1.00) during alcohol hangover. Conclusion. Hangover may impair specific cognitive functions, with implications for everyday task performance (e.g. attending work, driving). However, conclusions are tentative due to variability in methodologies of the studies reviewed.

Keywords: alcohol, hangover, cognition, psychomotor, sustained attention, memory, driving

3.2 Introduction

Research examining the cognitive effects of alcohol hangover have produced conflicting findings. Whilst, several studies report impairment in spatial and visual abilities (Kim, Yoon, Lee, Choi, & Go, 2003; Myrsten et al., 1970), attention (Anderson & Dawson, 1999; Howland et al., 2010; McKinney, Coyle, Penning, et al., 2012; Roehrs et al., 1991; Rohsenow et al., 2010), memory (Howland et al., 2010; McCaul et al., 1991; McKinney & Coyle, 2004, 2007; Verster et al., 2003), information processing speed (Anderson & Dawson, 1999; Grange et al., 2016), reaction times (Grange et al., 2016; McKinney & Coyle, 2004, 2007), and intellectual processes (Kim et al., 2003; Myrsten et al., 1970), others reveal no clear evidence that hangover affects cognition (Carroll et al., 1964; Chait & Perry, 1994; Collins, 1980; Collins & Chiles, 1978; Dowd et al., 1973; Finnigan et al., 1998, 2005a; Howland et al., 2010; Ideström & Cadenius, 1968; Lemon et al., 1993; Morrow et al., 1990; Myrsten et al., 1970; Rohsenow et al., 2010; Verster et al., 2003). Tasks reflecting workplace performance have also produced mixed results, with impairments in driving (Laurell & Tornros, 1983; Seppälå et al., 1976; Tornros & Laurell, 1991; Verster, Bervoets, et al., 2014), flying (Petros et al., 2003; Yesavage, Dolhert, & Taylor, 1994; Yesavage & Leirer, 1986), and surgical performance (Gallagher et al., 2011; Kocher, Warwick, Al-Ghnaniem, & Patel, 2006; Van Dyken, Szlabick, & Sticca, 2013), but not managerial decisions (Streufert et al., 1995) or problem solving in a ship engine (Rohsenow et al., 2006).

Disagreements in the definition of alcohol hangover may contribute to inconstancies with study designs and measures (Stephens et al., 2014, 2008). Some researchers argue that hangover constitutes any next-day effects following a night of heavy alcohol consumption, and often do not measure blood alcohol concentration (BAC) or hangover at the time of testing. However, some individuals may be hangover-resistant (Howland, Rohsenow, Allensworth-Davies, et al., 2008; Howland, Rohsenow, & Edwards, 2008; Verster, de Klerk, et al., 2014), experiencing no symptoms despite sufficient alcohol to induce hangover. Indeed, the importance of measuring hangover symptoms is

highlighted in a recent definition, which received consensus from academics in the field. It states hangover is a "combination of mental and physical symptoms, experienced the day after a single episode of heavy drinking, starting when BAC approaches zero" (van Schrojenstein Lantman, van de Loo, et al., 2017).

Peak BAC during a night of 'heavy' drinking may also contribute to conflicting results (Prat et al., 2008; Stephens et al., 2014). To induce a hangover, high amounts of alcohol (>1 g/kg) are consumed (Chapman, 1970), and the higher the amount, the more severe the cognitive impairments (Rohsenow et al., 2010). Hangovers are studied using either an experimental approach, where an alcohol challenge is administered, or using the naturalistic approach, where participants consume alcohol at a time and place typical for the individual. In experimental studies, hangover may not reliably be induced as practical and ethical issues could prevent doses > 1g/kg being administered - again highlighting the need to include measures of hangover in order to validate the hangover condition. Conversely, naturalistic studies have reported alcohol consumption at approximately 1.6g/kg (McKinney & Coyle, 2004), yet, unlike experimental studies, do not allow for the control of extraneous variables (e.g. food). Although naturalistic and experimental methods may reveal different impairments, it is important to assess convergence of findings across these different methodologies (Finnigan & Hammersley, 1992; Howitt & Cramer, 2007).

Previous reviews have highlighted other methodological limitations which contribute to conflicting findings, preventing firm conclusions (Frone & Verster, 2013; Gauvin, Cheng, & Holloway, 1993; Ling et al., 2010; Prat et al., 2008; Stephens et al., 2008). These include; no BAC measurement at testing, no counterbalance to avoid order effects, and poor controls of potentially confounding factors. These reviews excluded studies with BAC > 0 at testing (Ling et al., 2010; Prat et al., 2008; Stephens et al., 2008). However, alcohol hangover starts when BAC is *approaching* zero (van Schrojenstein Lantman, van de Loo, et al., 2017), indicating these reviews may have excluded potentially informative studies. As acute intoxication can produce cognitive

effects at BAC > 0.02%, studies which include participants above this threshold cannot disassociate hangover from acute intoxication effects.

The perspective taken here is that BAC should be < 0.02% at testing and hangover symptoms should be measured to validate the hangover condition. However, we acknowledge that, despite mean scores indicating higher hangover severity in hangover conditions, individuals within these groups may not experience hangover symptoms. As separate analysis is not typically reported for those with and without hangover following heavy alcohol consumption, this review should be regarded as examining next-day effects of heavy alcohol consumption. We acknowledge hangover has also been explored in animal models, however, the translational value of this work is currently unclear and so only human studies are included in this review.

To our knowledge, there have been no previous systematic reviews that have estimated mean effect sizes in a meta-analysis. This review aims to critically evaluate and estimate mean effect sizes to explore the next-day cognitive effects of heavy alcohol consumption.

3.3 Methods

3.3.1 Search Strategy and Inclusion Criteria

A literature search was conducted from December 2016 – May 2018 to identify studies examining the cognitive effects of alcohol hangover. PubMed, Embase, and PsycNET were searched using the strategy “alcohol” OR “ethanol” OR “alcohol intoxication” OR “alcohol drinking patterns” AND “hangover” OR “next day effects”. Search terms were adapted for each database and references searched for additional articles. Articles were screened by two independent reviewers and disagreements resolved by discussion in the first instance. If consensus was not reached, a third reviewer was consulted. The inclusion criteria for studies were developed based upon the consensus on hangover research report (Verster et al., 2010). Only studies that examined healthy human adults (18+ years of age) and contained a no-hangover control condition

were included in the review. Studies had to include a measure which validated the presence of hangover, such as a questionnaire assessing symptoms, and were required to report a BAC< 0.02% at testing. The inclusion criteria were based on a stringent set of criteria for hangover, however it is acknowledged that other approaches may be more inclusive of studies (e.g. including studies which do not include a measure of hangover or BAC at testing).

3.3.2 Data Extraction

Data were extracted from included studies for study design, cognitive tasks, hangover measurement, and BAC during hangover. Where possible, quantitative data were extracted and effect estimates calculated (Hunter & Schmidt, 2004; Lakens, 2013). Tasks were coded into their corresponding cognitive components (Selnes et al., 2007). Components and their sub-categories comprised of; Attention/Vigilance (selective, sustained, divided, and vigilance attention), Memory (working memory, short-term memory and long-term memory), and Psychomotor (speed and accuracy).

3.3.3 Data Analysis

All meta-analyses were performed using RevMan (RevMan, 2014). Hedges *g* effect size estimates were calculated for each outcome. For those studies with multiple outcomes in each category of cognition, effect sizes were averaged so that no study carried undue weight in determining overall effect. The weight given to each study was the inverse of the variance of the effect size, thus larger studies with smaller standard errors were given more weight.

3.4 Results

3.4.1 Identification of Studies

Agreement between reviewers was 95% with two ‘disagreements’ which were resolved through discussion, without the need to consult a third reviewer. In one case, upon both reviewers revisiting the paper, it was clear that the paper did not measure hangover. In the other case, inclusion criteria for one study were

reported across two papers. The reviewers agreed that the inclusion criteria were met by collating data from both papers.

The literature search identified 19 studies that could be included in the systematic review (Collins, 1980; Collins & Chiles, 1978; Finnigan et al., 2005a; Grange et al., 2016; Howland et al., 2010; Kim et al., 2003; Kruisselbrink et al., 2006; Laurell & Tornros, 1983; McKinney & Coyle, 2004, 2007; McKinney, Coyle, Penning, et al., 2012; Myrsten et al., 1970; Roehrs et al., 1991; Rohsenow et al., 2010, 2006; Streufert et al., 1995; Tornros & Laurell, 1991; Verster, Bervoets, et al., 2014; Verster et al., 2003), and 11 with sufficient data to be included in the meta-analysis (Grange et al., 2016; Howland et al., 2010; McKinney & Coyle, 2004, 2007; McKinney, Coyle, Penning, et al., 2012; Myrsten et al., 1970; Rohsenow et al., 2010; Verster et al., 2003). Of the 20 articles excluded during full text screening, 12 studies failed to measure hangover at testing, two of which (Gallagher et al., 2011) were reported in the same article (Hartung et al., 2015; Kocher et al., 2006; Lemon et al., 1993; Petros et al., 2003; Roehrs, Beare, Zorick, & Roth, 1994; Stock et al., 2017; Van Dyken et al., 2013; Wolff et al., 2016; Yesavage et al., 1994; Yesavage & Leirer, 1986). Two studies which included measures on subjective feelings during hangover, only found increases in fatigue or arousal (Chait & Perry, 1994; Finnigan et al., 1998) therefore it was unclear if participants were experiencing a hangover. Seven studies failed to measure BAC at testing (Anderson & Dawson, 1999; Gallagher et al., 2011; Hartung et al., 2015; Howse et al., 2018; McCaul et al., 1991; Petros et al., 2003; Yesavage et al., 1994), and two studies which did measure BAC, showed participants achieved BAC> 0.02% (Lemon et al., 1993; Seppälå et al., 1976). Two studies included other treatments in their research design (Chait & Perry, 1994; Myrsten et al., 1980). To avoid interference from either the substance or the placebo effect, these studies were excluded. Finally, a further study was excluded (McKinney, Coyle, & Verster, 2012) as the data analysed was already included in this review via another article from the same authors (McKinney & Coyle, 2004). Figure 3.1 represents a PRISMA diagram of study exclusion. Assuming studies which did not report participant attrition did not experience any, total participants recruited across all

included studies was 1163. The total number of participants for which data were reported was 846, an attrition rate of 27.3%.

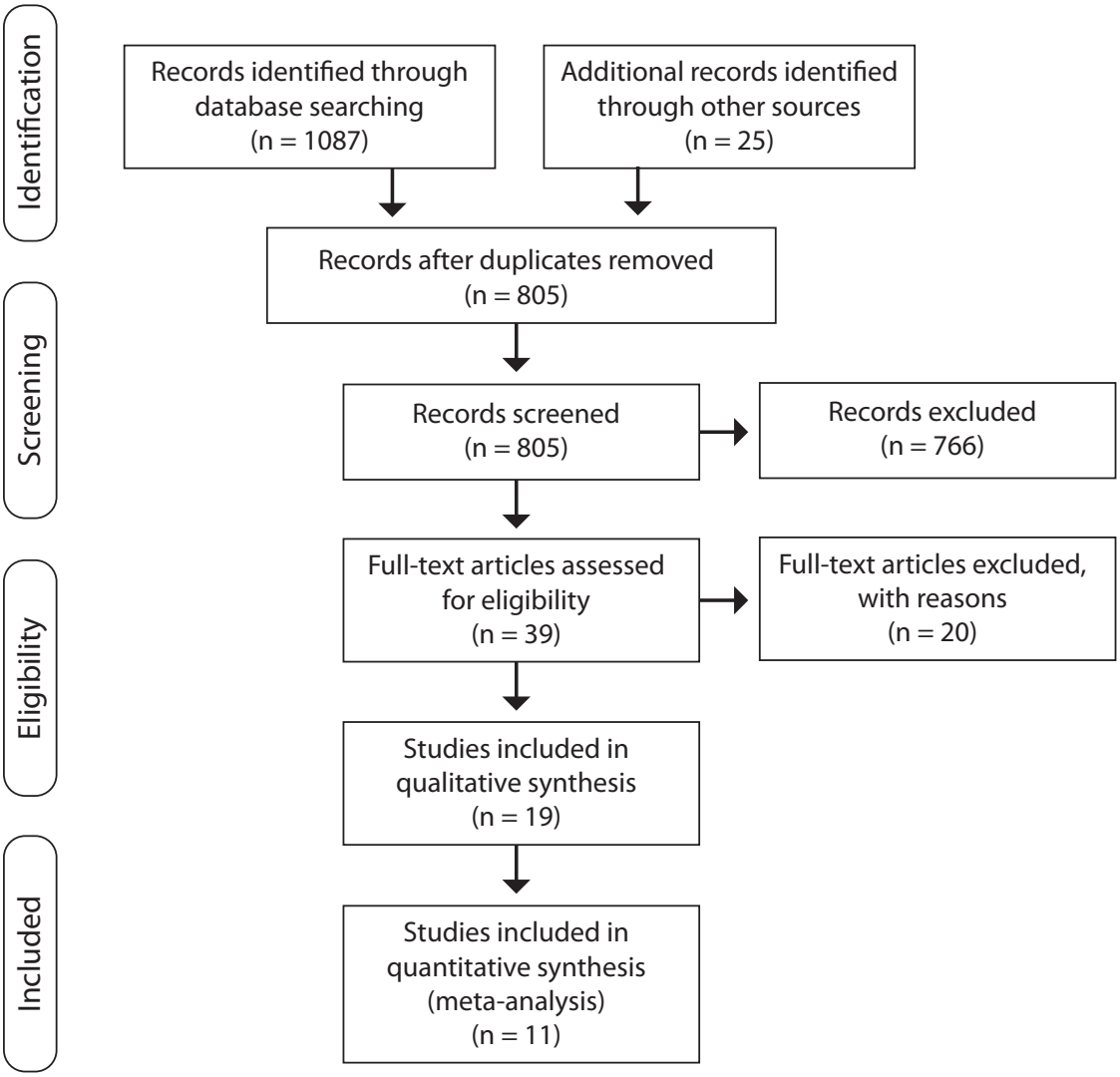


Figure 3.1. PRISMA Flow Diagram. 805 articles were screened by two independent reviewers, and 39 had full-text assessed. 19 articles were included in the review and 11 provided sufficient data to be included in meta-analysis

3.4.2 Included Studies

A total of 19 studies were included in the qualitative synthesis, as illustrated in Table 3.1. The 11 laboratory studies (Collins, 1980; Collins & Chiles, 1978; Howland et al., 2010; Kim et al., 2003; Kruisselbrink et al., 2006; Myrsten et al., 1970; Roehrs et al., 1991; Rohsenow et al., 2010, 2006; Streufert et al., 1995; Verster et al., 2003) typically administered lower doses of alcohol than were consumed during the 8 naturalistic drinking studies (Finnigan et al., 2005a; Grange et al., 2016; Laurell & Tornros, 1983; McKinney & Coyle, 2004, 2007; McKinney, Coyle, Penning, et al., 2012; Tornros & Laurell, 1991; Verster, Bervoets, et al., 2014; Verster et al., 2003). A total of 10 studies explored multiple aspects of cognition (Collins & Chiles, 1978; Finnigan et al., 2005; Howland et al., 2010; Kim et al., 2003; McKinney & Coyle, 2004, 2007; McKinney, Coyle, Penning, et al., 2012; Myrsten et al., 1970; Rohsenow et al., 2010; Verster et al., 2003). Risk of bias was assessed using RevMan (see Figure 3.2). One study did not sufficiently randomise to condition (Kim et al., 2003), and for all studies it was unclear whether there was bias for selective reporting due to a lack of study pre-registration. 50% of studies were at risk of other biases, including non-randomisation of task administration, and sampling biases. Blinding was not considered a risk of bias as participants readily guess conditions during experimental hangover research, despite blinding (Howland et al., 2010; Rohsenow et al., 2010).

Table 3.1. Description of included studies.

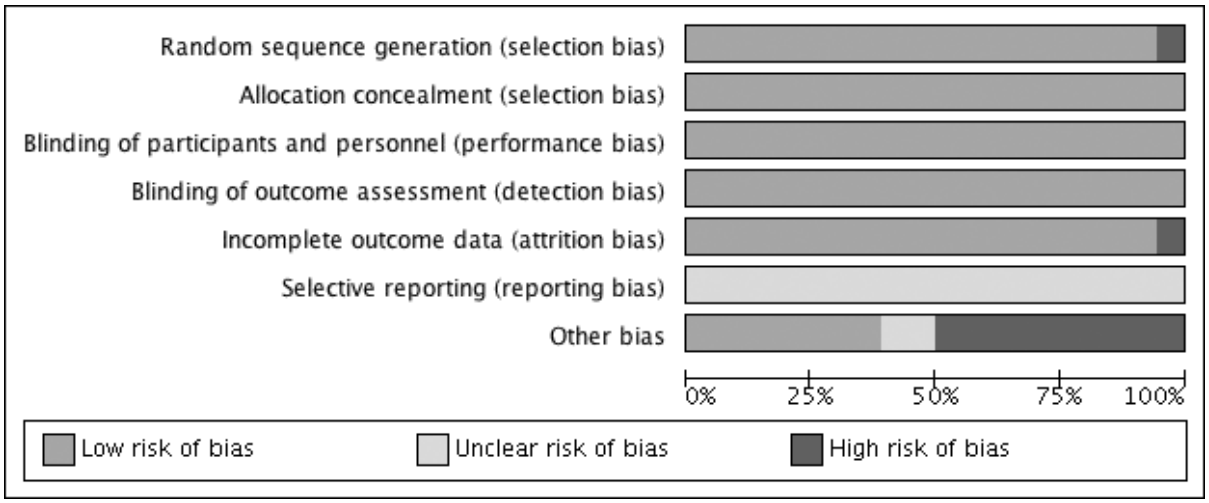
Study	n	Design	Alcohol	BAC at testing	Hangover measure	Tests Used	Cognitive Domain	Main Finding	Comments
Collins & Chiles, 1979	11	Within-subjects, Laboratory	13 g/kg	< 0.01%	20-item hangover questionnaire	Choice RT Meter Monitoring Pattern Identification Compensatory Tracking Problem Solving	P SA STM DA PS	Non-significant results	
Collins 1980	8	Within-subjects, Laboratory	1.3 g/kg	0.012%	20-item hangover questionnaire	Tracking task with RT	DA	Non-significant results	
Finnigan et al., 2005	71	2x3 mixed design, Naturalistic	1.77 g/kg	0%	Subjective feelings questionnaire	Psychomotor vigilance Dual task Probe memory recall	SA DA STM	Non-significant results	Group impaired in V, post-hoc significant for 'acute and hangover' only.
Grange et al., 2016	31	Within-subjects, Naturalistic	1.55 g/kg	0%	AHS	Choice RT	P	Impaired RT	Anecdotal evidence for impaired accuracy
Howland et al., 2010	184-193	Within-subjects, Laboratory	0.99 g/kg	0%	AHS	PVT CPT ADST-B APASAT VST-B PMT	SA SA WM WM WM STM	Impaired Non-significant Non-significant Non-significant Impaired Female only impairment	
Kim et al., 2003	13	Within-subjects, Naturalistic	1.5 g/kg	< 0.01%	Subjective Hangover Scale	LNNB	Various	Impairments in 'memory', 'Visual' and 'Intellectual' components	Excluded from meta-analysis as components cannot be sub-categorised
Kruisselbrink et al., 2006	12	Within-subjects, Laboratory	1.36 g/kg	0%	Rated common symptoms	Choice RT	P	Non-significant RT Impaired accuracy	Female participants Alcohol g/kg maximum dose

Laurell & Törnros, 1983	22	Within-subjects, Naturalistic	1.25 g/kg	0	Rated severity	Driving ability	RL	Impaired	
McKinney et al., 2004	48	Within-subjects, Naturalistic	1.54 g/kg	< 0.01%	Questionnaire on signs & symptoms	Free recall Delayed recognition Simple RT Choice RT	STM LTM P P	Impaired	STM impaired at 9:00 only, alcohol g/kg averaged male & female
McKinney et al., 2007	78	Mixed design, Naturalistic	1.67 g/kg	< 0.01%	Questionnaire on signs & symptoms	Free recall Delayed recognition Simple RT Choice RT	STM LTM P P	Impaired	Stressor between-subject condition. ES calculated for group effect (hangover/no-hangover). Alcohol g/kg averaged male & female
McKinney et al., 2012	48	Within-subjects, Naturalistic	1.54 g/kg	< 0.01%	Questionnaire on signs & symptoms	Sustained attention Divided attention Erikson Flanker Stroop Spatial attention	SA DA SelA SelA SpaA	Impaired Non-significant Impaired Impaired Non-significant	Alcohol g/kg averaged male & female
Mrysten et al., 1970	15	Within-subjects, Laboratory	1.43 g/kg	< 0.01%	Rated severity	Simple RT Choice RT F-Test Correction Test	P P EF SA	All non-significant except ‘spatial’ factor of F-Test	
Rohers et al., 1991	5	Within-subjects, Laboratory	0.8 g/kg	0%	Rated hangover	Divided attention	DA	Impaired tracking, but not RT	
Rohsenow et al., 2006	61	2x2 mixed, Laboratory	1.1 g/kg	< 0.02%	AHS	Simulated ship performance	PS	Non-significant	Outcome overall time. Alcohol g/kg averaged male & female
Rohsenow et al., 2010	89-95	2x2x2 mixed, Laboratory	1.15 g/kg	0	AHS	PVT CPT ADST-B APASAT VST-B PMT	SA SA WM WM WM STM	Impaired Impaired Non-significant Non-significant Non-significant Non-significant	Alcohol g/kg averaged male & female

Streufert et al., 1995	21	Within-subjects, Laboratory	1 g/kg	0	Drug effects questionnaire	Managerial simulations	EF	Non-significant	Involved decision making and planning
Törnros & Laurell, 1991	24	Within-subjects, Naturalistic	1.42 g/kg	< 0.02%*	Rated severity	Driving speed	RL	Non-significant	overall impaired, post-hoc BAC< 0.02% non-significant
Verster et al., 2003	48	Within-subjects, Naturalistic	1.4 g/kg	0	Severity scored	Immediate recall Delayed recall Delayed recognition Macworth Clock	STM LTM LTM VA	Non-significant Impaired Non-significant Non-significant	46 participants completed memory tasks
Verster et al., 2014	42	Within-subjects, Naturalistic	1.55 g/kg	< 0.01**	Severity scored	Driving ability	RL	Ability impaired Speed non-significant	Alcohol g/kg averaged male & female

P = Psychomotor, SA = Sustained Attention, DA = Divided Attention, SelA = Selective Attention, SpaA = Spatial Attention, VA = Vigilance Attention, STM = short-term memory, LTM = Long-term memory, WM = Working memory, PS = Problem solving, EF = Executive Function (non-specified), RL = 'Real-Life', AHS = Acute Hangover Scale, *BAC > 0.02% at 9am session, **BAC> 0.02% for 4 participants, however inclusion did not impact results (correspondence with authors).

Figure 3.2. Risk of Bias Graph



One study was at risk of insufficient randomisation procedures, all studies were at risk of reporting bias as there were no pre-registered study protocols, and 50% of studies were at risk of biases such as non-randomised task order and sampling bias.

3.4.3 Attention

Sustained Attention. Five studies explored sustained attention, three laboratory (Howland et al., 2010; Myrsten et al., 1970; Rohsenow et al., 2010), and two naturalistic (Finnigan et al., 2005; McKinney, Coyle, Penning, et al., 2012). Howland et al. (2010), McKinney et al. (2012), and Rohsenow et al. (2010) reported impairments, whereas Finnigan et al. (2005), and Mrysten et al. (1970) showed no evidence of next-day effects on sustained attention . Two studies used tasks from a tool validated for assessing cognitive impairments: the neurobehavioural evaluation system-3 (Howland et al., 2010; Rohsenow et al., 2010; White et al., 2003), two used a sustained attention task which presented stimuli at a consistent rate and participants responded to consecutive stimuli (Finnigan et al., 2005; McKinney, Coyle, Penning, et al., 2012), and one used a 'correction test' where participants marked identical rows in a list of two columns (Myrsten et al., 1970). Four studies provided sufficient information to be included in the meta-analysis (Howland et al., 2010; McKinney, Coyle, Penning, et al., 2012; Myrsten et al., 1970; Rohsenow et al., 2010), which revealed an overall impairment in sustained attention during hangover (g = 0.47, 95% CI 0.07 to 0.87, I^2 = 50%). This is shown graphically in Figure 3.3.

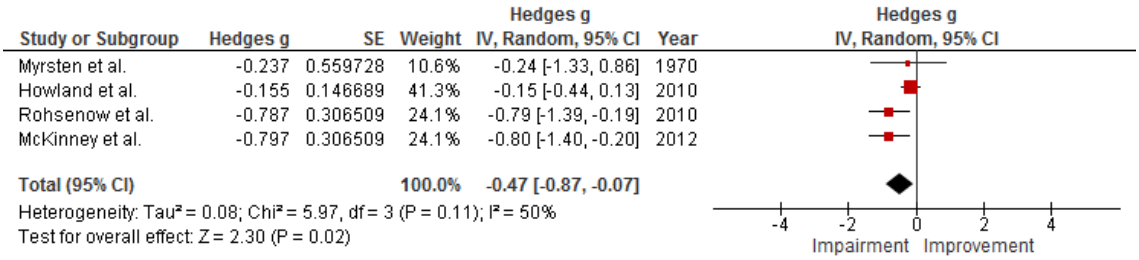


Figure 3.3. Forest Plot for Sustained Attention. Testing for an overall effect revealed a significant impairment (p=0.02) with a small to medium effect estimate of 0.47, 95% CI 0.07 to 0.87.

Divided Attention. Five studies included measures of divided attention (Collins, 1980; Collins & Chiles, 1978; Finnigan et al., 2005; McKinney, Coyle, Penning, et al., 2012; Roehrs et al., 1991). Of these, one (with a small sample size; *n* = 5) reported impairments in divided attention (Roehrs et al., 1991). The four other studies showed no evidence of a next-day effect on divided attention. Four studies were included in a meta-analysis (Collins, 1980; Collins & Chiles, 1978; McKinney, Coyle, Penning, et al., 2012; Roehrs et al., 1991) which showed no evidence of a next-day effect on divided attention.

Other Attention. Verster et al. (2003) analysed vigilance using the Macworth clock test and found no evidence of next-day effects. McKinney et al. (2012) found slowed reaction times (RT) for both near and far distractors in a selective attention task, and increased interference the day after heavy alcohol consumption in the Stroop test. As only one study explored vigilance, and only one explored selective attention, a meta-analysis was not performed for these categories of attention.

3.4.4 Memory

Short-Term Memory. Short-term memory (STM) was assessed in seven studies (Collins & Chiles, 1978; Finnigan et al., 2005; Howland et al., 2010; McKinney & Coyle, 2004, 2007; Rohsenow et al., 2010; Verster et al., 2003), three naturalistic (Finnigan et al., 2005; McKinney & Coyle, 2004, 2007) and four laboratory (Collins & Chiles, 1978; Howland et al., 2010; Rohsenow et al., 2010; Verster et al., 2003). McKinney and Coyle (2004, 2007), and Howland et al.

(2010) reported impairments, with Howland et al. showing a female only impairment, whereas Collins and Chiles (1978), Finnigan et al. (2005), Rohsenow et al. (2010), and Verster et al. (2003) reported no evidence of a next-day effect. Three studies used a word recall task (McKinney & Coyle, 2004, 2007; Verster et al., 2003), one used a similar task which measured probed recall (Finnigan et al., 2005), two used a pattern memory test (Howland et al., 2010; Rohsenow et al., 2010), and one used a 'pattern identification task' (Collins & Chiles, 1978). Five studies provided sufficient information to be included in the meta-analysis (Collins & Chiles, 1978; Howland et al., 2010; McKinney & Coyle, 2004, 2007; Verster et al., 2003), which, as indicated in figure 3.4, revealed an overall impairment for STM during hangover (*g* = 0.64, 95% CI 0.15 to 1.13, I^2 =73%).

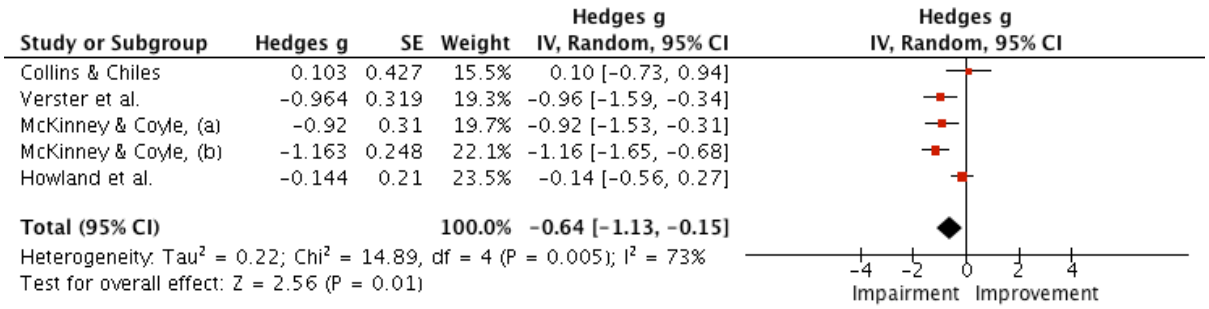


Figure 3.4. Forest Plot for Short-Term Memory. Testing for an overall effect revealed a significant impairment (p=0.01) with a medium effect estimate of 0.64, 95% CI 0.15 to 1.13.

Long Term Memory. Four studies, two naturalistic (McKinney & Coyle, 2004, 2007) and two laboratory (Howland et al., 2010; Verster et al., 2003), assessed long-term memory (LTM). Verster et al., (Verster et al., 2003) and McKinney and Coyle (2004; 2007) used a word recall task and reported impairments in LTM. However, in Howland et al. (2010), where participants were required to learn lecture materials pre-intoxication, there was no evidence of a next-day effect on LTM. Figure 3.5 shows that when all 4 studies were included in a meta-analysis, there was an overall impairment in LTM during hangover (*g* = 0.59, 95% CI 0.01 to 1.17, I^2 =84%).

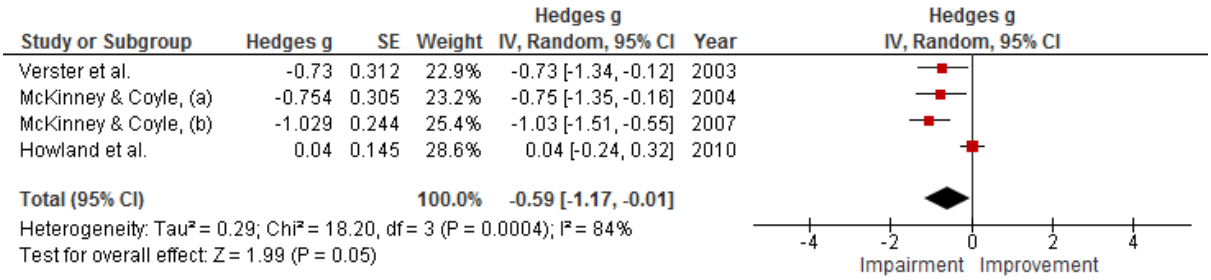


Figure 3.5. Forest Plot for Long-Term Memory. Testing for an overall effect revealed a significant impairment (p=0.05) with a medium effect estimate of 0.59, 95% CI 0.01 to 1.17.

Other Memory. Howland et al. (2010) and Rohsenow et al. (2010) investigated working memory using the adaptive paced auditory serial addition test (APASAT), the visual span-backwards (VST-B) and the auditory digit span-backwards (ADS-B). They found no evidence of a next-day effect in the APASAT or the ADS-B, however, Howland et al. (2010) reported impairments in the VST-B during hangover. Kim et al. (2003) also reported impairments in the memory domain of the Luria-Nebraska Neurobehavioural Battery (LNNB), however as this domain encompasses STM, LTM and working memory (Golden, Hammeke, & Purisch, 1978), it is unclear which aspects of memory were impaired.

3.4.5 Psychomotor Performance

Speed. Psychomotor speed was measured using reaction time (RT) in six studies (Collins & Chiles, 1978; Grange et al., 2016; Kruisselbrink et al., 2006; McKinney & Coyle, 2004, 2007; Myrsten et al., 1970). Three naturalistic studies (Grange et al., 2016; McKinney & Coyle, 2004, 2007) found slower RT the day after an evening of heavy alcohol consumption, whereas three laboratory studies found no evidence to support this (Collins & Chiles, 1978; Kruisselbrink et al., 2006; Myrsten et al., 1970). Five studies (Collins & Chiles, 1978; Grange et al., 2016; McKinney & Coyle, 2004, 2007; Myrsten et al., 1970) were included in the meta-analysis, which, as shown in Figure 3.6, indicated that psychomotor speed was slowed the following day (g = 0.66, 95% CI 0.31 to 1.00, I^2 =36%).

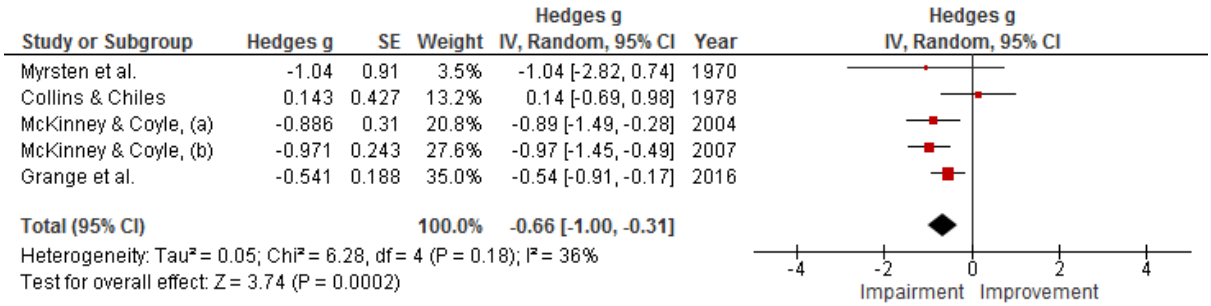


Figure 3.6. Forest Plot for Psychomotor Speed. Testing for an overall effect revealed a significant impairment (p=<0.001) with a medium effect estimate of 0.66, 95% CI 0.31 to 1.00.

Accuracy. Two studies reported psychomotor accuracy (Grange et al., 2016; Kruisselbrink et al., 2006). Kruisselbrink et al. (2006) found a decrease in psychomotor accuracy following an evening of heavy alcohol consumption, whereas Grange et al. (2016) reported no evidence of an effect on accuracy.

3.4.6 'Real-Life' Simulations

Six studies included a 'real-life' simulation that required cognitive performance. Rohsenow et al. (2006) reported no evidence of an effect for solving a mechanical failure during a simulated ship scenario. Streufert et al. (1995) reported no clear evidence of an effect on performance in scenarios which require managerial skills, and Howland et al. (2010) reported no evidence of a next-day effect for General Record Examination scores on two factors; verbal and quantitative. For studies that analysed driving following an evening of heavy alcohol consumption (Laurell & Tornros, 1983; Tornros & Laurell, 1991; Verster, Bervoets, et al., 2014), the ability to control a vehicle, as measured by deviation from a set course, was impaired (Laurell & Tornros, 1983; Verster, Bervoets, et al., 2014), whereas there was no clear evidence to suggest a next-day effect on driving speed (Tornros & Laurell, 1991). Due to considerable differences in research methodology it was not possible to conduct a meta-analysis for 'real-life' simulations.

3.5 Discussion

The systematic review and meta-analyses indicate that STM, LTM sustained attention and psychomotor speed are impaired the day after an evening of heavy alcohol consumption. Results were mixed for the impact of next-day effects on working memory, and there was no clear evidence of an effect on divided attention or vigilance, suggesting that specific components of cognition are influenced the next day. The meta-analysis showed that psychomotor speed, STM, and LTM had medium overall effect estimates (g = 0.66, g = 0.64, and g = 0.59 respectively), and sustained attention had a small effect estimate (g = 0.47).

Our systematic review indicated that sustained attention was impaired in studies using naturalistic and laboratory methodologies, with meta-analysis revealing an overall impairment with a small effect size (g = 0.47). For divided attention, only Rohers et al. (1991) reported an impairment; however, the reliability of this study is potentially limited by the small sample size (n = 5). Meta-analysis data revealed no evidence of a next-day effect on divided attention. Next-day impairments in sustained attention may reflect accumulating mental fatigue, induced by prolonged attentional demands (Langner, Willmes, Chatterjee, Eickhoff, & Sturm, 2010). Fatigue is a common symptom of hangover (Penning, McKinney, & Verster, 2012b) and involves reward-cost trade-offs (Boksem et al., 2005; Boksem & Tops, 2008). Therefore, hangover-induced fatigue may contribute to impairments observed in sustained attention. The lack of clear evidence for an effect in some studies of sustained attention may reflect insensitivity of the cognitive task used. Studies which used tasks that have not previously demonstrated sensitivity to state changes in drug use (Collins, 1980; Collins & Chiles, 1978; Myrsten et al., 1970) tended to report no evidence of a next-day effect, whereas studies (McKinney, Coyle, Penning, et al., 2012) that used cognitive tasks that have previously detected state changes (Tiplady et al., 2001), were more likely to report next-day related impairments. Next-day effects on sustained and divided attention may also have been masked by low statistical power. For example, Finnigan et al. (2005) had small, unequal group sizes in their between-subjects design (n = 13, n = 25, n = 33 for ‘acute and hangover’, hangover, and control groups respectively).

Our review highlights converging evidence from both methodologies (experimental and naturalistic) that STM and LTM may be influenced the morning following a night of heavy alcohol consumption, with the meta-analysis revealing impairments in both. It is possible that memory formation, rather than retrieval, may be affected as indicated by the differential next-day effects on studies in which learning took place following heavy alcohol consumption versus sober state. An important process for memory formation in the hippocampus is long-term potentiation (LTP) - the strengthening of signals between neurons (Carter & Murphy, 1999). Given the detrimental effect of elevated IL-6 (Bellinger, Madamba, Campbell, & Siggins, 1995; Li, Katafuchi, Oda, Hori, & Oomura, 1997; Tancredi & D'Antuono, 2000), and cortisol (Monk & Nelson, 2002) on LTP (Balschun et al., 2004), and the increase of these in the morning following heavy alcohol consumption (Kim et al., 2003; Linkola et al., 1979; A Van de Loo et al., 2015), this could be a possible mechanism underlying next-day related impairment of memory formation. Three studies examined memory processes using a naturalistic methodology, two of which reported impairments in STM and LTM, whereas Finnigan et al. (2005) reported no evidence of impairments in STM. However, as mentioned above, this study may have lacked the statistical power to identify next-day effects. Experimental studies on the other hand, have largely reported no evidence of next-day impairment of memory, although studies where participants reached higher BACs tended to report impairments (Howland et al., 2010; Verster et al., 2003). As with studies of attention, some studies that reported no clear evidence of an effect on memory may have used tasks that are insensitive to the acute next-day effects.

Systematic review revealed conflicting results for next-day influences on psychomotor speed. However, when effect estimates were combined in the meta-analysis, there was an overall impairment with a medium effect estimate (g = 0.66). It is important to consider the suitability of RT as an outcome measure when assessing the next-day effects on cognition. For example Howland et al. (2010) and Rohsenow et al. (2010) use RT as an outcome measure in tasks of sustained attention. Both reveal impairments, however, it is

unclear whether the impairment is related to sustained attention, or psychomotor speed. Some cognitive tasks of sustained attention, which do not use RT as an outcome measure, revealed no clear evidence of next-day effects on attention (Myrsten et al., 1970). Three naturalistic studies reported slower RTs, whereas three laboratory studies reported no evidence of an effect, although Kruisselbrink et al. (2006) reported decreased accuracy. Studies using experimental manipulation of 'hangover' typically administered lower doses of alcohol than studies where 'hangover' occurred "naturally" (1.3-1.43 g/kg, and ~1.54-1.67 g/kg respectively), and had smaller sample sizes (*n* = 8-12) which may impact reliability (Button et al., 2013). It should be noted, that due to insufficient information, one laboratory study (Kruisselbrink et al., 2006) could not be included in the meta-analysis, which may over-inflate the effect estimate reported.

Three naturalistic studies identified in this review assessed driving the morning following a night of heavy alcohol consumption. Verster et al. (2014) and Laurell and Törnros (1983) reported impairments in ability to control the vehicle. However, Törnros and Laurell (1991) reported that no effect on speed the next-day. These studies have important implications for road safety, especially given that hangover may contribute to road-traffic accidents (Hoiseth, Fosen, Liane, Bogstrand, & Morland, 2015). The impairments observed in ability to drive may be driven by next-day effects on underlying cognitive components. Driving uses psychomotor speed and sustained attention (Allen et al., 2009), both of which appear to be impaired in this review. Studies using experimental manipulation of hangover, which assessed task performance using measures of executive function (problem solving, and decision-making), as well as academic performance, all found no clear evidence of a next-day effect. However, an outcome measure of overall completion time, as in Rohsenow et al. (2006), and the managerial task used in Streufert et al. (1995) may not be sufficient to detect next-day effects. Together, these findings echo the recommendations of previous reviews (Prat et al., 2008; Stephens et al., 2008), indicating that further research is needed to determine hangover effects on executive functions. We also suggest that future studies of executive function should use validated

measures known to be sensitive to state changes in drug use, such as the Iowa Gambling Task (Bechara, Tranel, & Damasio, 2000).

In line with previous reviews (Ling et al., 2010; Prat et al., 2008; Stephens et al., 2014, 2008), this systematic review and meta-analysis revealed several methodological issues which limit the interpretation of evidence from studies of alcohol hangover on cognition. Although the studies included in this review met rigorous criteria, there was a high degree of variability in the design of individual studies, possibly reflected by the high level of heterogeneity observed. Our review highlights that low sensitivity of tasks to detect next-day impairments may underlie null next-day effects on cognition. The use of cognitive tasks sensitive to state changes in substance use is essential for studies exploring cognitive effects the day after a night of heavy alcohol consumption (Parrott, 1991). Thought should also be given to the sensitivity of visual stimuli to next-day effects, as opposed to auditory stimuli. Studies using cognitive tasks with auditory stimuli revealed no evidence of a next-day effect on cognition in contrast to effects observed when using visual stimuli. This discrepancy is supported by evidence of impairments of the 'visual' component of the LNNB task battery (Kim et al., 2003). Another factor that may influence the next-day effect on cognition is study design. Our review suggests a greater likelihood of next-day impairment in studies of naturalistic design. In studies where hangover is induced "naturally", alcohol consumption was higher (mean alcohol dose 1.54 g/kg) than in experimental studies (mean alcohol dose 1.21 g/kg). This finding suggests that higher alcohol doses are associated with greater next-day performance impairments (Liu & Ho, 2016).

Finally, several other limitations should be considered. One study (Kim et al., 2003) did not randomise condition order, whilst others did not randomise task administration order (McKinney & Coyle, 2004, 2007; McKinney, Coyle, Penning, et al., 2012). Randomisation to condition is important to prevent practice effects, and randomising task order limits confounding variables such as fatigue. Several studies did not control for nicotine use (Collins, 1980; Collins & Chiles, 1978; Myrsten et al., 1970), which is known to influence cognitive

performance (Swan & Lessov-Schlaggar, 2007). Our review also highlighted variability between study design in the amount of time between alcohol consumption and cognitive testing, possibly depriving participants of sleep. Sleep time is an important consideration when researching cognition as cognitive components are differentially affected by sleep loss (Jackson et al., 2013). Although in real-life drinking some individuals may reduce sleep time for drinking time (Verster, 2008), variability between studies for the time allowed for sleep make it difficult to draw firm conclusions regarding cognitive effects.

Based on these shortcomings, we make the following recommendations for future research. First, to address the shortcoming of low statistical power, studies should conduct a-priori power analysis to determine an estimate of required sample sizes. Second, studies should adopt tasks that have been validated and shown to be sensitive to state changes in drug use. Third, consideration should be given for the use of RT as an outcome measure in tasks, and interpretation should acknowledge the potential impact of next-day psychomotor impairments. Fourth, future research should seek to address the paucity of robust research examining executive functions the morning following a night of heavy alcohol consumption.

3.6 Conclusion

To our knowledge, this study is the first to systematically review the literature exploring next-day effects on cognitive performance and to estimate mean effect sizes. Our review reveals next-day impairments in STM, LTM, psychomotor speed, and sustained attention, with mixed findings for next-day effects on working memory, and no clear evidence of an effect on divided attention. Results from our meta-analysis indicate medium effect sizes for psychomotor speed, STM, and LTM, and a small effect size for sustained attention. These findings suggest that specific cognitive functions may be impaired the morning following a night of heavy alcohol consumption, with implications for everyday task performance (e.g. driving).

3.7 Commentary Text

Results from the systematic review indicate that core cognitive functions, such as sustained attention, memory, and psychomotor skills are impaired during hangover. However, the review also highlights that few studies have investigated the influence of hangover on higher thought processes, such as executive functions. As hangover has previously been associated with the development of alcohol use disorder (Courtney et al., 2018; Piasecki et al., 2010), subsequent experimental work (Chapter Five) will investigate the effect of hangover on cognitions that contribute toward alcohol-seeking behaviours. Specifically, the cognitions to be investigated will be response inhibition and attentional bias towards alcohol-related stimuli (M. Field et al., 2010; Goldstein & Volkow, 2002; Jentsch & Taylor, 1999).

To investigate the effect of alcohol hangover on attentional bias towards alcohol-related stimuli, a Visual Dot Probe task (VDP) will be used, which has been utilised in previous studies investigating attentional bias in adult social drinkers (Adams et al., 2012). However, to improve the reliability of this task, it is first important to develop an effective stimulus set. Therefore, the development of this stimulus set is outlined in Chapter Four before the presentation of experimental work in Chapter Five.

Chapter 4: The Development of Picture-Pair Sets for use in a Visual Dot Probe Task

4.1 Introduction

Visual Dot Probe (VDP) tasks have been used to assess attentional bias in a variety of different research topics (Pool, Brosch, Delplanque, & Sander, 2016; Yiend, 2010), including alcohol attentional bias (see Field and Cox, 2008). The task aims to capture preferential processing of emotionally relevant stimuli and typically involves the presentation of two pictures or words on-screen simultaneously, followed by a 'probe', which participants are required to respond to. For alcohol research, picture sets are typically comprised of alcohol-related images matched with neutral images. Findings from studies that adopted this task have indicated that preferential processing of alcohol-related stimuli occurs in heavy social drinkers (M. Field, Mogg, Zetteler, & Bradley, 2004) and during intoxication (Adams et al., 2012). These results have contributed to the theory that the preferential processing of alcohol-related stimuli contributes to the development of alcohol use disorder (M. Field et al., 2010). However, recently researchers have questioned the internal reliability of cognitive bias tests in general (Ataya et al., 2012a, 2012b; Christiansen, Mansfield, Duckworth, Field, & Jones, 2015) and much is unknown about how factors within visual stimuli (e.g., novelty) influence attentional bias (Miller & Fillmore, 2010). To improve reliability and reduce potential influence of factors within visual stimuli, it is important to use eye-tracking alongside VDP tasks (Christiansen *et al.*, 2015), and to produce a quality picture set that controls perceptual content. The study presented in Chapter Five addresses the aim of investigating the effects of alcohol hangover on response inhibition and attentional bias towards alcohol-related stimuli by utilising a VDP task. Although the study in Chapter Five tried to achieve the best reliability by using eye-tracking alongside the development of an appropriate stimulus set, due to technical difficulties, eye-tracking data was unusable. Nonetheless, the current chapter outlines the creation and validation of an appropriate stimulus set to improve reliability of the VDP task.

Effective picture sets utilised for VDP tasks match both images in a picture pair on perceptual characteristics, such as brightness, luminance, and complexity. As a picture pair contains an alcohol-related and neutral image that are presented simultaneously, differences in factors other than content, such as luminance, colour and form, could draw attention (Turatto & Galfano, 2000). For example, if the neutral image in a picture pair was brighter than the alcohol image, attention could be drawn toward this image irrespective of content. In turn, this would cause faster reaction times to the neutral image, which could then be incorrectly interpreted as an attentional bias. Another important factor for the creation of picture sets is complexity. Some studies have included complex scenes with multiple items in the visual display (e.g., Duka & Townshend, 2004; M. Field, Mogg, & Bradley, 2005), whereas other studies have included singular objects (e.g. Adams et al., 2012; Miller & Fillmore, 2010). Despite the argument that complexity reflects real-life, and are therefore ecologically valid (e.g., in a supermarket aisle there could a variety of different items), picture sets of low complexity are more effective at revealing attentional bias (Miller & Fillmore, 2010). Therefore, an optimal picture set to use with the VDP task is one of low complexity and matched perceptual characteristics.

In addition to matching picture pairs on perceptual characteristics and complexity, it is important to match picture pairs on factors relating to content, such as semantic category, novelty, and emotional content. As alcohol-related pictures belong to one semantic category, it is recommended that the neutral stimuli belong to one category too (Cox, Pothos, Johnsen, & Laberg, 2001). Further, as novelty captures attention (Johnston, Hawley, Plewe, Elliott, & DeWitt, 1990), stimuli should avoid being highly novel to avoid misinterpretation of preferential processing of stimuli due to novelty as an alcohol-related attentional bias. Thus, both picture types (alcohol-related and neutral) should be tailored to be easily recognisable to participants when completing the VDP task. For alcohol-related images, novelty can be reduced by using popular branded products (e.g., Carlsberg lager). Participants that will complete the VDP task in Chapter Five will be recruited from university staff and students. As university staff and students would be familiar with office-based items, images from the semantic category ‘stationary’ will be used for neutral stimuli. However, there

are also recommendations for the control of emotional content of picture pairs in VDP tasks (Bauer & Cox, 1998; Robbins & Ehrman, 2004), and arguably alcohol-related images would differ in emotional content to 'stationary' images. Despite the previous use of the category 'stationary' in VDP tasks (Duka & Townshend, 2004), it is important to validate picture pairs to ensure emotional content is matched. Validation of picture pairs would also ensure novelty and perceptual characteristics such as similarity are matched.

The main aim of the current chapter was to develop a set of simple alcohol-related and neutral (stationary) picture pairs that were matched for perceptual characteristics, emotional content, and novelty. Picture pairs were presented to friends and colleagues in order to assess similarity in these characteristics. These picture pairs will be utilised in a VDP task to measure attentional bias toward alcohol-related stimuli in the experimental work described in Chapter Five.

4.2 Methods

4.2.1 Participants

Friends and colleagues (*n* = 10) were used to rate these pictures. All were social drinkers aged 18 – 30 who regularly experienced hangovers. These criteria are similar to the main criteria for participants that participated in the research utilising the picture-pair sets developed in the current study.

4.2.2 Picture Creation

Photographs were taken using an Olympus E-510 Digital Single-Lens Reflex (DSLR) camera. The DSLR camera was placed on a tripod 80cm away from the object and 90cm from the ground. The object was placed on a surface 68cm from the ground which had been covered in a black cloth to create a black background. To control for brightness and luminance the object had two studio lamps placed at a height of 140cm to the left of the camera, and 108cm to the right of the camera.

A total of 64 (32 alcohol-related, 32 neutral) pictures were edited and rated. Image brightness and sharpness were edited using Adobe Photoshop from Adobe Creative Suite version CS5.5 on a Mac Mini 2.6 GHz Intel Core i7 with macOS Sierra. Images were matched based on perceptual characteristics judged by 2 ‘experts’ (a researcher from the University of Bath, and a Graphic Designer).

4.2.3 Selection of Alcohol-related Images

To decrease the chance of alcohol-related images appearing novel, products were selected based on popular brand names. Perceptual characteristics and content were also matched to neutral stimuli. 13 beer products, 8 wine products, and 11 ‘other’ alcoholic beverages (9 spirits and 2 alcopops) were selected. These products were pictured alone, or alongside glasses or other products relating to their consumption (e.g., a pint glass next to beer product). The wine products were chosen to reflect the various types of wine available; white, red, rosé and prosecco.

4.2.4 Selection of Neutral Images

Neutral images were all selected from the category of ‘stationary’. Perceptual characteristics and content were matched to alcohol-related stimuli. Where multiple objects were used, these were placed in such a way that would enable a ‘single’ visual display (see Figure 2.1). This was to allow colour matching without compromising complexity.

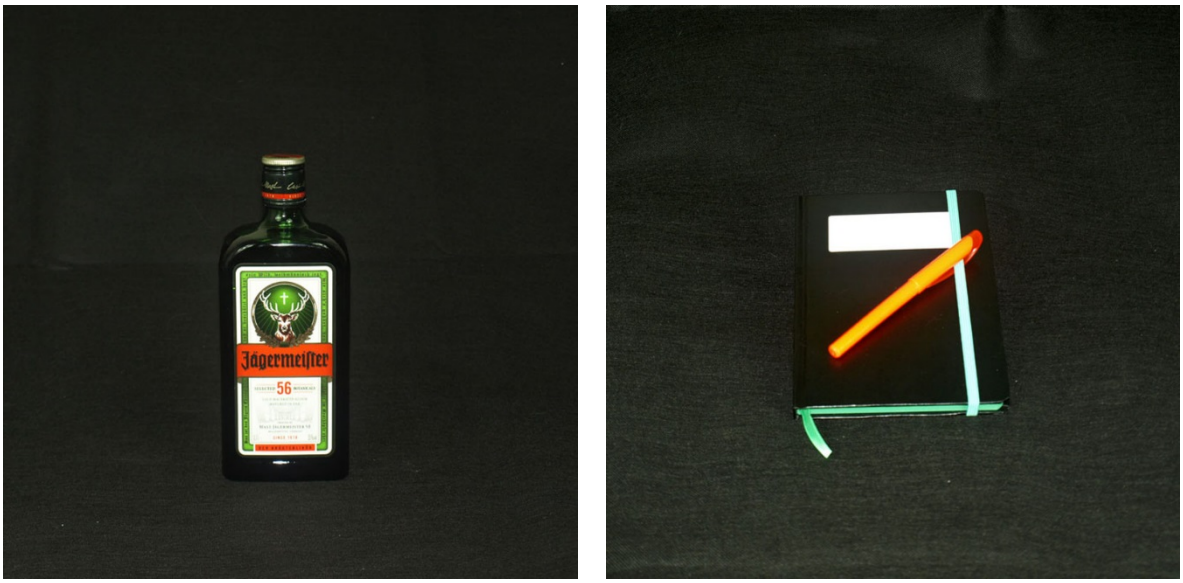
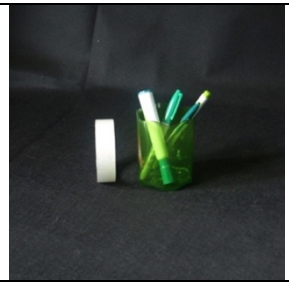


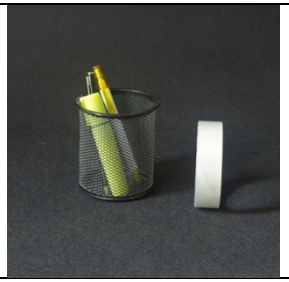
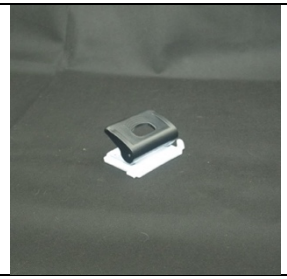
Figure 2.1. Example of inclusion of multiple images creating a single visual display

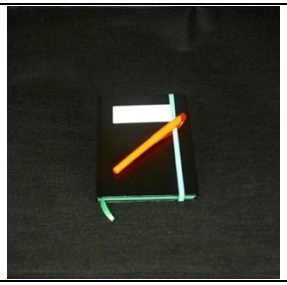
4.2.5 Stimuli Rating Task

Images were displayed side by side in a Qualtrics survey. Participants were asked to rate their agreement, ranging from strongly agree – strongly disagree on a 5-point Likert scale, with 5 statements relating to the paired images. For each individual image, statements concerned emotional content, valence, alcohol-relatedness, and novelty. The statements were; 'I like the content of the [RIGHT/LEFT] image', 'I find the [RIGHT/LEFT] image pleasurable', 'The content of the [RIGHT/LEFT] image is alcohol related', 'The content of the [RIGHT/LEFT] image is novel'. Participants also rated agreement for a statement relating to both images on similarity, 'The content of the two images look similar' (see Table 2.1).

Table 2.1 The final picture set of 12 stimulus-pairs

				
	San Miguel	**Neutral San Miguel**	**Budweiser**	**Neutral Budweiser**
The content of the images look similar	3		3	
I like the content of the image	3	3	3	3
I find the content of the image pleasurable	3	3	3	3
The content of the image is alcohol-related	5	1	5	1
The content of the image is novel	2	2	2	2
				
	Carling	**Neutral Carling**	**Carlsberg & Glass**	**Neutral Carlsberg & Glass**
The content of the images look similar	4		3	
I like the content of the image	3	3	3	3
I find the content of the image pleasurable	3	3	3	3
The content of the image is alcohol-related	5	1	5	1
The content of the image is novel	2	2	2	2

				
	Fosters	**Neutral Fosters**	**Prosecco**	**Neutral Prosecco**
The content of the images look similar	3		3	
I like the content of the image	3	3	3	3
I find the content of the image pleasurable	3	3	3	3
The content of the image is alcohol-related	5	1	5	1
The content of the image is novel	2	2	2	2
				
	Red Wine	**Neutral Red Wine**	**Rosé Wine**	**Neutral Rosé Wine**
The content of the images look similar	3		3	
I like the content of the image	3	3	4	3
I find the content of the image pleasurable	3	3	4	3
The content of the image is alcohol-related	5	1	5	1
The content of the image is novel	2	2	2	2

				
	White Wine	**Neutral White Wine**	**Jägermeister**	**Neutral Jägermeister**
The content of the images look similar	3		3	
I like the content of the image	4	3	4	3
I find the content of the image pleasurable	3	3	3	3
The content of the image is alcohol-related	5	1	5	1
The content of the image is novel	2	2	2	2
				
	WKD	**Neutral WKD**	**WKD Blue**	**Neutral WKD Blue**
The content of the images look similar	4		3	
I like the content of the image	4	4	3	3
I find the content of the image pleasurable	3	3	3	3
The content of the image is alcohol-related	5	1	5	1
The content of the image is novel	2	2	2	2

4.2.6 Data Analysis

Mean scores were calculated for each of the ratings for each picture. To be included in the final picture-pair set, images had to match or have scores between 2 – 4 and within 1 point of each other on the questions; 'I like the content of the image', and 'I find the content of the image pleasurable'. Scores also had to be ≤ 2 on the question 'I find the content of the image is novel' for both images in the pair. For the alcohol-related images, scores had to be '5' for the question 'The content of the image is alcohol-related', and the matched neutral image had to score '1'. Images also had to be ≥ 4 for 'The content of the two images look similar'. These inclusion criteria were modelled after Adams (2011) Unpublished thesis "Effects of Acute Alcohol Consumption on Impulsivity and Motivational Salience for Alcohol Cues in Light and Heavy Social Drinkers" University of Bristol.

4.3 Results & Discussion

Only 2 picture pairs met the criteria for 'The content of the two images look similar', which contrasted with the consensus of 'expert' judgements. It is possible that the wording of the statement that was used in the stimulus rating task was too ambiguous. By 'content' the intention was for participants to judge the picture pairs on perceptual content (i.e., colour and complexity). However, 'content' could include sematic categories, and so the statement may have been interpreted as making a judgement as to whether an alcohol-related object (e.g., can of Carlsberg) was similar to a 'stationary' object (e.g., a pot of pens). Due to this limitation, it would not be appropriate to use results from this statement for the creation of the final picture set. Therefore, the final picture-set was developed based on ratings that met criteria for the remaining four statements.

In total, 19 picture pairs met the criteria for inclusion in the final picture-pair set. As only 12 picture-pairs were needed for the VDP task, the final images were chosen to reflect a variety of types of beverages. Therefore, the final 12 matched pairs contained 5 images of beers, 4 images of wines, and 3 images of 'other' (spirits and alcopops; Figure 2.2).

In conclusion, the current chapter developed a set of 12 validated picture-pairs matched on perceptual characteristics and factors related to content. These picture pairs are thus appropriate for use in the VDP task that will be used to measure attentional bias towards alcohol-related stimuli during alcohol hangover (Chapter Five).

Chapter Five: The Effects of Alcohol Hangover on Response Inhibition and Attentional Bias towards Alcohol-Related Stimuli

Declaration of Authorship

This declaration concerns the article entitled:			
The Effects of Alcohol Hangover on Response Inhibition and Attentional Bias towards Alcohol-Related Stimuli			
Publication status (tick one) **Draft manuscript** [ ] **Submitted** [X] **In review** [ ] **Accepted** [ ] **Published** [ ]			
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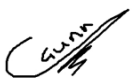
Copyright status (tick the appropriate statement) I hold the copyright for this material [X] Copyright is retained by the publisher, but I have been given permission to replicate the material here [ ]			
Candidate's contribution to the paper (provide details, and also indicate as a percentage)	The candidate contributed to / considerably contributed to / predominantly executed the… Formulation of ideas: Predominantly executed Design of methodology: Predominantly executed Experimental work: Predominantly executed Presentation of data in journal format: Considerably contributed		
Statement from Candidate	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature.		
Signed		**Date**	13/02/2020

The Effects of Alcohol Hangover on Response Inhibition and Attentional Bias towards Alcohol-Related Stimuli

Craig Gunn[1], Joris C. Verster[2,3,4], Graeme Fairchild[5], and Sally Adams[1]

[1] Addiction and Mental Health Group, Department of Psychology, University of Bath, Bath, UK.

[2] Division of Pharmacology, Utrecht University, 3584CG Utrecht, The Netherlands

[3] Institute for Risk Assessment Sciences (IRAS), Utrecht University, 3584CM Utrecht, The Netherlands

[4] Centre for Human Psychopharmacology, Swinburne University, Melbourne, VIC 3122, Australia

[5] Department of Psychology, University of Bath, Bath, UK

Corresponding author: Craig Gunn, Addiction and Mental Health Group, Department of Psychology, University of Bath, Bath, BA2 7AY, United Kingdom. E: c.a.gunn@bath.ac.uk

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Running Head: Inhibition and Attentional Bias in Hangover

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5.1 Abstract

Background and Aims

Alcohol hangover is associated with the development of alcohol use disorders. Whilst impaired response inhibition and enhanced attentional bias for alcohol-related stimuli are established as mechanisms underlying the effects of acute alcohol intoxication on continued alcohol use, few studies have examined these cognitive processes during hangover. Therefore, the current study aimed to explore the effects of hangover on response inhibition and attentional bias for alcohol-related stimuli.

Design

A within-subjects, crossover 'naturalistic' design was utilised. Participants completed measures of response inhibition and attentional bias on a morning following alcohol consumption (hangover condition) and a morning following no alcohol consumption for at least 24 hours (no-hangover condition). Condition order was randomised and counterbalanced across subjects.

Setting

Department of Psychology, University of Bath, UK

Participants

Thirty-seven adult drinkers (predominantly undergraduate students) who reported regularly engaging in heavy episodic drinking and experiencing a hangover at least once in the previous month.

Measurements

Primary outcomes were commission errors on the Go/No-Go task, and attentional bias scores on the Visual Dot Probe task. Participants also completed measures of hangover severity, and VAS-mood (pre- and post-task), sleep, alcohol craving, and perceived mental effort scales.

Findings

Participants displayed impaired response inhibition during hangover compared to the no-hangover condition ($p < .001$, $d = 0.89$), but there were no differences in attentional bias scores between conditions. Participants reported expending

greater mental effort to complete tasks during hangover compared to the no-hangover condition (p < .001, d = 1.65). They also reported decreased alertness (p < .001, d = 3.19), and feelings of tranquillity (p < .001, d = 1.49) in the hangover versus no-hangover condition.

Conclusions

Alcohol hangover appears to impair response inhibition, negatively impact mood, and increase perceived mental effort to complete cognitive tasks, but does not influence attentional bias for alcohol-related cues.

Keywords: Alcohol, Hangover, Cognition, Attentional Bias, Mood, Response Inhibition

5.2 Introduction

The most commonly reported negative consequence following a night of heavy alcohol consumption is alcohol hangover (McGee & Kypri, 2004). Alcohol hangover is defined as a "combination of mental and physical symptoms that occur the morning after a night of heavy alcohol consumption, when blood alcohol concentration (BAC) approaches zero" (van Schrojenstein Lantman, van de Loo, et al., 2017). Alcohol-related absenteeism, which includes hangover, costs the UK economy £1.9 billion per annum, yet its impact on productivity is still unknown (Bhattacharya, 2017). Hangover may also increase the risk of developing alcohol use disorders. The development of alcohol use disorder has been linked to hangover frequency whilst controlling for previous drinking behaviour, indicating that hangover uniquely contributes towards problem drinking (Courtney et al., 2018; Molbak, Schou, & Tolstrup, 2017; Piasecki et al., 2010). However, the mechanisms underlying the association between alcohol hangover and the development of alcohol use disorders are not well understood. One hypothesis is that alcohol hangover leads to impairments in response inhibition and attentional biases towards alcohol-related stimuli.

Enhanced salience of alcohol and alcohol-related stimuli, combined with reduced inhibitory control, has been theorised to contribute toward the development of alcohol use disorders (M. Field et al., 2010; Goldstein & Volkow, 2002; Jentsch & Taylor, 1999). Studies of acute intoxication indicate that following an alcohol prime, alcohol-related stimuli gain strong motivational properties and receive preferential attentional processing (i.e. attentional bias) (Duka & Townshend, 2004; M. Field et al., 2005). In turn, attentional bias contributes toward alcohol-seeking behaviours and in the long-term to the development of alcohol use disorders (M. Field & Cox, 2008; Robinson & Berridge, 1993; Rooke, Hine, & Thorsteinsson, 2008). However, attentional bias toward alcohol-related stimuli may also differ according to drinking status, with heavy social drinkers exhibiting an enhanced attentional bias towards alcohol-related cues than light drinkers (Adams et al., 2012; Bruce & Jones, 2004; M. Field et al., 2004; Jones, Bruce, Livingstone, & Reed, 2006; Ryan, 2002; Townshend & Duka, 2001). Similarly, reduced response inhibition is also

observed in acute intoxication (De Wit, Crean, & Richards, 2000; Marczinski, Abroms, Van Selst, & Fillmore, 2005) and appears to contribute towards poor decision-making in recently detoxified alcohol dependent individuals (Noël, Bechara, Dan, Hanak, & Verbanck, 2007). Greater impairment in inhibitory control whilst intoxicated is also associated with increased ad-lib alcohol consumption when sober (Weafer & Fillmore, 2008), highlighting that poorer inhibitory abilities may contribute toward future alcohol consumption. Furthermore, alcohol-induced impairments in inhibitory control are enhanced when alcohol-related stimuli are used as targets (Adams, Ataya, Attwood, & Munafò, 2013; Noël et al., 2007; Weafer & Fillmore, 2012). Alongside enhanced salience of alcohol and alcohol-related cues and poorer inhibition, models of alcohol use disorder highlight that negative affect can increase alcohol-seeking behaviours via negative reinforcement (Koob, 2013). Together these studies suggest that poor response inhibition, enhanced attentional biases towards alcohol-related stimuli, and negative affect are risk factors for problematic alcohol use. Although previous studies have reported an increase in negative affect during hangover (McKinney, 2010), few studies have examined response inhibition and attentional biases during hangover.

Therefore, it is not known whether hangover influences attentional bias towards alcohol-related stimuli. One possibility based on anecdotal evidence (e.g. “I’ll never drink again”) is that alcohol-related cues – being related to the substance that caused the discomfort – are viewed as aversive. Animal studies have also lent support to the notion that consuming alcohol is aversive during a hangover. Gauvin et al. (1997) trained rats to drink alcohol freely before injecting them with a high dose of alcohol. Consumption of alcohol decreased during the hangover stage, suggestive of avoidance. However, social drinkers mention using alcohol as a treatment for hangover, which may be effective to some extent as an individual returns to an intoxicated state (Verster, 2009). In addition, avoidance of alcohol during hangover may be influenced by drinking status. For example, one study reported that 25% of students who experience hangovers have attempted to use alcohol to ‘cure’ their hangover, and this behaviour was associated with heavier alcohol consumption in the future (Hunt-Carter et al., 2005). Furthermore, those who used alcohol to relieve hangover symptoms

were more likely to meet diagnostic criteria for an alcohol use disorder. Thus, the extent to which an individual avoids alcohol-related stimuli during a hangover may be related to their drinking status (heavy versus light social drinker).

Previous studies have utilised tasks of interference control – another form of inhibition (Devenney et al., 2019; Devenney & Verster, 2019; Friedman & Miyake, 2004; McKinney, Coyle, Penning, et al., 2012; Zink et al., 2018), and one recent study has investigated the effects of hangover on response inhibition (Opitz et al., 2019). Three naturalistic studies asked participants to complete the Eriksen Flanker and Stroop tasks, measuring different aspects of interference control, in two conditions; the morning after a night of naturalistic drinking (hangover), and again after no alcohol consumption (no-hangover) (Devenney et al., 2019; Devenney & Verster, 2019; McKinney, Coyle, Penning, et al., 2012). In one study, student participants who were experiencing a hangover exhibited greater impairments in interference control on both tasks compared to the no-hangover condition (McKinney, Coyle, Penning, et al., 2012), whilst another found impairments on the Stroop task only (Devenney & Verster, 2019). In contrast, a naturalistic study that recruited participants from the general population showed no hangover effects on interference control on either task (Devenney et al., 2019). One study that experimentally induced hangover also found no evidence of hangover-related effects on interference control using the Eriksen Flanker task (Zink et al., 2018). Further, a recent study that experimentally induced hangover found a slight impairment in response selection, but not response inhibition (Opitz et al., 2019). Thus, there is a need for greater clarity regarding the effects of hangover on inhibitory processes, and a need to understand the effect of hangover following naturalistic drinking on inhibitory processes other than interference control (i.e., response inhibition). Given that response inhibition is impaired in the majority of acute studies (M. Field et al., 2010) and interference control has been observed to be impaired in naturalistic hangover (Devenney & Verster, 2019; McKinney, Coyle, Penning, et al., 2012), it is hypothesised that response inhibition would be impaired during naturalistic hangover.

The current study aimed to compare response inhibition and attentional bias towards alcohol-related stimuli, between hangover and no-hangover conditions. As a secondary aim, we investigated mood and broader subjective effects of hangover. Specifically, our hypotheses were: 1) participants will exhibit poorer response inhibition in the hangover compared to no-hangover condition; 2) individuals will exhibit attentional avoidance toward alcohol-related stimuli in the hangover compared to the no-hangover condition; and 3) attentional avoidance toward alcohol-related stimuli in the hangover condition will correlate negatively with self-reported alcohol use (i.e., it will be stronger in lighter drinkers). Our secondary hypotheses were: 1) hangover severity will be positively related to response inhibition impairments and the degree of attentional avoidance and 2) mood will be reduced and perceived effort will be increased in the hangover compared to no-hangover condition.

5.3 Methods

5.3.1 Participants

Using an effect size of $\eta_p^2 = 0.172$ for increased distractor interference during hangover (McKinney et al. 2012), a G-power (Faul, Erdeilder, Lang, & Buchner, 2007) analysis was conducted to determine an a-priori sample size for the current study. Analysis suggested 34 participants would be needed to determine an effect of response inhibition across two conditions (hangover, no-hangover) with 0.90 power and an alpha level of 0.05. Allowing for attrition, this study aimed to recruit 40 participants (20 male, 20 female).

Fifty-nine non-smoking, healthy volunteers, aged 18–30 years old, who experienced a hangover in the past month, and consumed > 6 (female) or > 8 (male) units of alcohol on their 'typical' night of heavy drinking were recruited predominantly from a student population for this study. Thus, participants in this study were not hangover-resistant, and regularly consumed the amount of alcohol likely to produce a hangover. Participants who consumed > 400mg caffeine per day were excluded to avoid the possibility that acute caffeine withdrawal effects would confound performance on the cognitive tasks. Additionally, participants were not pregnant/breastfeeding, had

normal/corrected-to-normal vision, had no current/past personal/family history of alcohol/drug dependency, and had no diagnosed sleep disorder. Twenty-two participants withdrew (21 following screening, 1 following no-hangover testing), thus 37 participants completed the study. The University of Bath's Psychology Research Ethics Committee approved this research (Ethics Code: 17-080).

5.3.2 Design

A within-subjects crossover 'naturalistic' design was utilised, whereby participants were randomised to either the hangover (morning following alcohol consumption) or no-hangover condition (after at least 24 hours of no alcohol consumption) first.

5.3.3 Measures

The Go/No-Go task was used as a measure of response inhibition (Bezdjian, Baker, Lozano, & Raine, 2009). Participants were presented with a 2x2 grid with a star in each section. Participants responded as quickly and accurately as possible to one of two targets ('Go' or 'No-Go') by pressing the spacebar for the 'Go' target, or withholding a response to the 'No-Go' target. 'Go' and 'No-Go' targets appeared 80% and 20% of the time, respectively. The task consisted of two blocks, with 20 practice trials and 160 experimental trials per block. In the first block, the letter 'P' was the 'Go' target and 'R' was the No-Go. This was reversed in the second block. In each trial, targets randomly replaced one of the stars for a duration of 500ms followed by an inter-stimulus interval of 1500ms. The primary outcome measure was commission errors – failure to withhold a response to 'No-Go' targets.

The Visual Dot Probe (VDP) task was used to measure attentional bias toward alcohol-related stimuli alongside eye-tracking to improve internal validity (Christiansen et al., 2015). Participants were asked to respond as quickly and accurately as possible to a visual probe (circle/square) by pressing the up or down arrows. There were 12 stimulus pairs, consisting of alcohol-related images matched on perceptual characteristics (i.e., colour and complexity) with neutral stimuli from the category 'stationery'. At the beginning of each trial a

fixation cross, presented in the middle of the screen, was replaced after a stable eye fixation period of 500ms by a stimulus pair (1 alcohol-related, 1 neutral) for 500ms, displayed side by side. A probe replaced one of the stimuli and participants were given 2500ms to respond, after which there was an inter-trial interval of 500ms. There were eight practice trials and 192 experimental trials presented in two blocks (96 trials per block). Probes replaced alcohol-related and neutral stimuli with equal frequency, and equally on each side of the screen. The 12 picture pairs appeared 16 times each, in equal frequency in each location (8 left, 8 right). Errors were removed and reaction time (RT) for correct responses to probes were used to calculate attentional bias scores, as per (M. Field et al., 2005). Eye-tracking data were collected, but due to technical errors, the data were unusable and are therefore not reported here. Figure 5.1 shows a schematic representation of the Go/No-Go and VDP tasks.

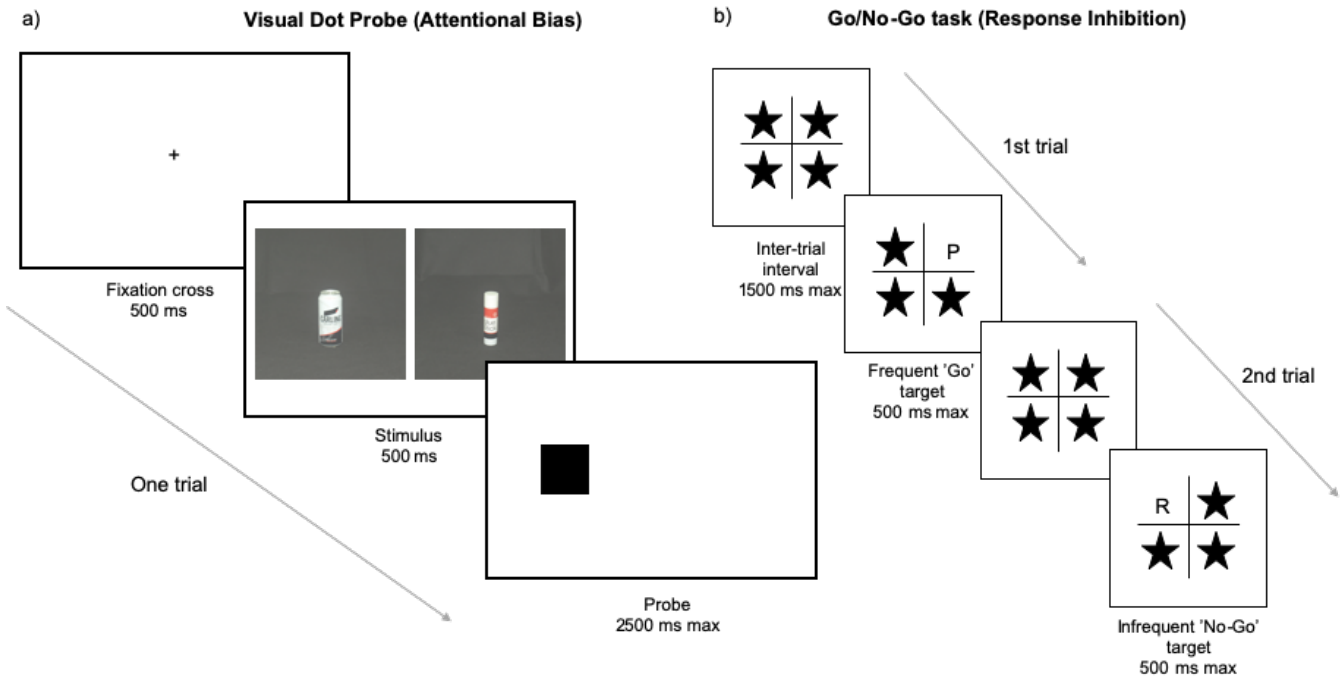


Figure 5.1. Schematic representations of the neurocognitive tasks used in this study. a) Schematic representation of the Visual Dot Probe task measuring attentional bias towards alcohol-related stimuli. Participants are presented with a fixation cross followed by a pair of images, one alcohol-related (a beer care on the left in this example) and one neutral (right in this example). The images are then replaced by a probe (circle or square), to which participants respond by pressing the up or down arrow on the keyboard. b) Schematic representation of the Go/No-Go task used to measure response inhibition. Participants are presented with a 2x2 grid of stars. One of these stars is replaced by a target stimulus and participants respond by pressing the space bar for 'Go' stimuli ('P') or withholding their response to 'No-Go' stimuli ('R').

During screening, participants completed the Barratt Impulsivity Scale-11 (BIS-11; (Patton, Stanford, & Barratt, 1995), a risk-taking questionnaire (RT-18; de Haan et al., 2011), the trait dimension of the State-Trait Anxiety Inventory (STAI; Lushene, Gorsuch, & Spielberger, 1970), and the Alcohol Use Disorder Identification Test (AUDIT; Babor, Higgins-Biddle, Saunders, & Monteiro, 1992). Estimated Blood Alcohol Concentration (eBAC) for 'typical' heavy drinking session was also calculated at screening using the Widmark formula (Kypri et al., 2005).

At both test sessions, alcohol consumption was self-reported from the previous night using pictorial prompts labelled with alcohol unit content to enable calculation of eBAC. Participants also completed the modified Alcohol Hangover Severity Scale (mAHSS), a 1-item hangover severity scale (Aurora Van de Loo et al., 2017), Groningen Sleep Quality Scale (GSQS; Mulder-Hajonides van der Meulen WREH, Wijnberg JR, Hollander JJ, De Diana IPF, 1980), Karolinska Sleepiness Scale (KSS; Åkerstedt & Gillberg, 1990), and the Alcohol Urges Questionnaire (AUQ; Bohn, Krahn, & Staehler, 1995). Participants completed mood visual analogue scales (VAS; Bond & Lader, 1974) before and after the cognitive tests, and completed the rating scale of mental effort (RSME; Zijlstra & Van Doorn, 1985) to assess perceived mental effort during cognitive tasks.

5.3.4 Procedure

Participants attended a screening session to ensure they met the inclusion criteria, provided informed consent, and completed baseline questionnaires (BIS-11, RT-18, STAI, AUDIT). Participants were randomised to a condition order (i.e., hangover first, no-hangover first) in a within-subject design, and booked two sessions (hangover and no-hangover) according to their anticipated drinking pattern. The time of day of testing was similar for both conditions.

On the morning of both sessions, participants were instructed to abstain from caffeine (verified by self-report) and nicotine consumption (verified by exhaled carbon monoxide < 10 ppm). As BAC levels > 0.02% can produce cognitive

effects reflective of acute alcohol intoxication (Holloway, 1994), participants were breathalysed in both conditions to confirm BAC was ≤ 0.02% before testing began. Participants then completed pre-task questionnaires (KSS, GSQS, a 1-item hangover severity scale, mAHSS, AUQ, VAS) before the Go/No-Go and VDP tasks in a counterbalanced order. Following the cognitive tasks, participants completed post-task measures (VAS, RSME). Upon completion of both conditions, participants were paid £15 and received a full debrief.

5.3.5 Statistical Analysis

Attentional bias scores were calculated by subtracting mean RTs to probes replacing alcohol-related images from mean RTs to probes replacing neutral images, in line with (M. Field et al., 2005). Outliers were removed from data if they were > 1.5*inter-quartile range and > 2 *SD* from the mean. Outliers were also removed from the VDP task if RTs were < 200 or > 2000ms (Ratcliff, 1993). Screening identified one outlier for Go/No-Go commission errors, and four outliers for VDP attentional bias scores. For VAS mood data, the 2 factors 'alertness' and 'tranquillity' were calculated as per (Herbert, Johns, & Doré, 1976). The factor 'alertness' comprised items such as 'lethargic/energetic' and 'alert/drowsy', and the factor 'tranquillity' comprised items such as 'happy/sad' and 'calm/excited'. We modified the statistical analysis from that specified in the pre-registered plan (Gunn, Griffin, Verster, & Adams, 2017) because the data were not suitable for ANCOVA analysis. Repeated measures analyses of variance (ANOVA) were performed using SPSS (version 24). Initially, order was included in the model as a between-subjects factor for all analyses. However, order was removed from the model if there was no evidence of it interacting with the other variables. Where data were non-normally distributed, bootstrapping of 5000 samples was performed (A. P. Field, 2018).

5.4 Results

5.4.1 Participant characteristics

Table 5.1 shows the participants' demographic and clinical characteristics. Mean age of participants was 20.22 years (*SD* = 2.2; range = 18 - 28) and

mean AUDIT score was 12.75 (*SD* = 3.96; range = 6 – 22). The mean number of units of alcohol consumed and eBAC reported at screening for a 'typical' heavy drinking episode were 15.05 (*SD* = 5.41) and 0.17% (*SD* = 0.06; range = 0.09% – 0.3%) respectively.

Table 5.1. Demographic characteristics of the sample and descriptive statistics regarding their alcohol consumption

Measures	**Total**	**37**	
	Male	19	
	Female	18	
		Mean	**SD**
Age (years)	Total	20.22	2.2
	Male	19.47	2.2
	Female	20.22	2.68
AUDIT	Total	12.75	3.96
	Male	13.32	3.79
	Female	12.12	4.17
'Typical' heavy drinking eBAC	Total	0.17	0.06
	Male	0.17	0.06
	Female	0.17	0.05
'Typical' heavy drinking units	Total	15.05	5.41
	Male	17.49	5.14
	Female	12.48	4.5
Previous night heavy drinking eBAC	Total	0.17	0.05
	Male	0.17	0.06
	Female	0.17	0.05
Previous night heavy drinking units	Total	14.75	5.64
	Male	17.68	5.86
	Female	11.66	3.35

Note. SD, Standard deviation; AUDIT, Alcohol Use Disorder Identification Test; eBAC, estimated Blood Alcohol Concentration

5.4.2 Alcohol Consumption Prior to Hangover Condition

Participants consumed an average of 14.75 (*SD* = 5.64) units of alcohol, reaching an average eBAC of 0.17% (*SD* = 0.05) on the night before the hangover testing session. Units of alcohol consumed and eBAC did not significantly differ between the night before the hangover session and self-reported 'typical' drinking occasions (*p*s ≥ .40); indicating that taking part in the study did not influence or change participants' typical alcohol consumption.

5.4.3 Effects of Hangover on Response Inhibition

A paired samples t-test indicated that participants made more commission errors ($t(35) = 3.73$, $p = .001$, CI [2.00 – 6.44], $d = 0.62$) in the hangover condition ($M = 20.61$, $SD = 11.31$) than the no-hangover condition ($M = 16.33$, $SD = 9.18$; Figure 5.2).

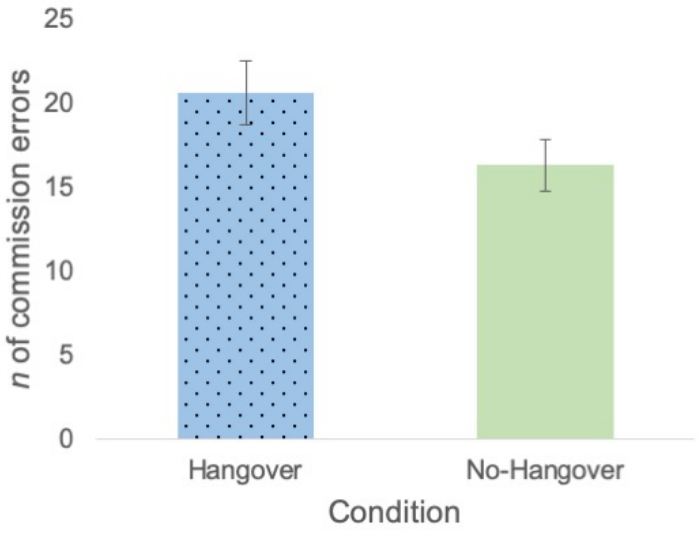


Figure 5.2. Mean number of commission errors on the Go/No-Go task in the hangover versus the no-hangover condition. A greater number of commission errors were made in the hangover condition compared to the no-hangover condition indicating poorer response inhibition in hangover. Error bars represent ±1 standard error of the mean.

5.4.4 Effect of Hangover on Attentional Bias

Attentional bias scores were calculated in line with (M. Field et al., 2005), whereby positive scores indicate attention towards alcohol, and negative scores indicate avoidance from alcohol-related images. Mean (SD) attentional bias scores in the hangover and no-hangover conditions were 0.34ms (2.93) and 3.96ms (2.12) respectively. A repeated measures ANOVA showed no main effects of condition or interactions between condition and order on attentional bias scores (*ps* > .31; Figure 5.3).

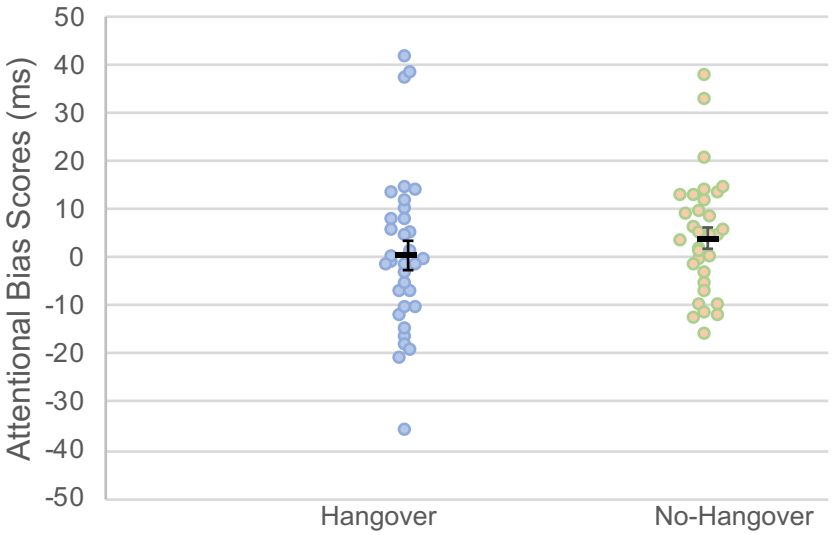


Figure 5.3. Scatter plot showing attentional bias scores for each condition. Each dot represent an individual participant's score. Black bars indicate mean attentional bias scores. Error bars represent ±1 standard error of the mean.

5.4.5 Correlations

Commission errors in the hangover condition were not correlated with alcohol consumption: AUDIT (r = -.04, p = .81) or either measure of hangover severity: mAHSS (r = -.08, p = .63) or 1-item hangover severity scores (r = -.15, p = .36). Attentional bias scores were not correlated with alcohol consumption (AUDIT) or hangover severity (mAHSS or 1-item hangover severity), rs ≤ .12, ps ≥ .51.

5.4.6 Subjective Questionnaires

Repeated measure ANOVAs were conducted separately for alertness and tranquillity factors. For alertness, there was a main effect of condition (F(1, 33) = 83.99, p < .001, d = 3.19), whereby participants were less alert in the hangover condition (M = 45.49, SE = 0.67) than in the no-hangover condition (M = 54.72, SE = 0.67). This difference had a very large effect size. There was also strong evidence for a condition*time interaction (F(1,33) = 12.04, p = .001, d = 1.21), driven by an increase in alertness scores from pre- to post-test in the hangover condition and a decrease in alertness scores from pre- to post-test in the no-hangover condition. Further, there was an order*time interaction (F(1, 35) = 4.29, p = .046, d = 0.64), which was explained by participants showing lower post-test alertness scores when they completed the no-hangover condition first. For tranquillity scores, there was a main effect of condition (F(1, 33) = 18.22, p < .001, d = 1.49), such that tranquillity was lower in the hangover (M = 44.34, SE = 0.6) than the no-hangover condition (M = 47.83, SE = 0.68). However, there was no effect of time or condition*time interaction (ps > .38).

Separate paired t-tests indicated greater sleepiness (t(33) = 12.74, p < .001, d = 2.19), poorer sleep quality (t(34) = 8.09, p < .001, d = 1.37), greater perceived mental effort to complete tasks (t(36) = 7.09, p < .001, d = 1.17), and fewer urges to consume alcohol (t(35) = -2.39, p = .023, d = 0.4) in the hangover compared to the no-hangover condition (see Table 5.2).

Variable	Test	*n*	Hangover		No-Hangover		Statistic	*p*	Effect size
			Mean	(SD)	Mean	(SD)			
Response Inhibition	Commission errors	36	20.61	(11.31)	16.33	(9.18)	t = 3.728	.001	d = 0.62
Attentional Bias	AB scores	33	0.34	(2.93)	3.96	(2.12)	F = 1.054	.312	d = 0.36
Hangover Severity	mAHSS	35	3.2	(1.37)	0.31	(0.32)	t = 13.155	< .001	d = 2.22
	1-item hangover severity	35	5.51	(1.85)	0.09	(0.51)	t = 15.795	< .001	d = 2.66
Mood	Alertness	35	45.49	(0.67)	54.72	(0.67)	F = 83.991	< .001	d = 3.19
	Tranquillity	35	44.34	(0.6)	47.83	(0.68)	F = 18.218	< .001	d = 1.49
Mental Effort	RSME	37	76.68	(25.18)	47.55	(22.23)	t = 7.09	< .001	d = 1.17
Alcohol Craving	AUQ	36	9.81	(3.76)	11.72	(4.81)	t = -2.39	.023	d = 0.4
Sleep	KSS	34	6.53	(1.08)	3.56	(1.16)	t = 12.74	< .001	d = *2.19*
	GSQS	35	6.54	(2.28)	2.51	(2.2)	t = 8.09	< .001	d = 1.37

Table 5.2. Descriptive statistics for the cognitive tasks and questionnaires in the hangover and no-hangover conditions

Note. SD, Standard deviation; AB, Attentional bias; mAHSS, modified Alcohol Hangover Severity Scale; RSME, rating scale of mental effort; AUQ, Alcohol Urges Questionnaire; KSS, Karolinska Sleepiness Scale; GSQS, Groningen Sleep Quality Scale.

5.5 Discussion

Our results suggest that participants show poorer response inhibition when experiencing a hangover, compared to when they are not hungover. Contrary to our hypothesis, there was no evidence that hangover influenced attentional bias, either in terms of avoidance or approach towards alcohol-related stimuli. Also contrary to our hypotheses, there was no relationship between attentional bias scores and levels of alcohol consumption, and no evidence that hangover severity was associated with commission errors or attentional bias scores. Secondary findings from our study revealed that participants experienced decreased alertness and tranquillity, and reported that they needed to expend greater mental effort to complete the cognitive tasks when experiencing a hangover compared to the no-hangover condition.

Our results are consistent with previous naturalistic hangover studies showing poorer interference control during hangover (Devenney & Verster, 2019; McKinney, Coyle, Penning, et al., 2012). Together, these findings suggest that individuals are less able to inhibit pre-potent responses during hangover. This is consistent with effects observed during acute intoxication (M. Field et al., 2010), suggesting that the effects of alcohol on inhibitory control continue into the hangover stage. It is important to highlight that our findings, although consistent with other studies of naturalistic hangover, are in contrast to recent studies that experimentally induced hangover. Following administration of a set dose of alcohol to induce hangover (achieved BAC 0.11%), no evidence of hangover-related impairments in interference control were observed when completing the Eriksen Flanker task (Zink et al., 2018). Further, another study that administered a set dose of alcohol (achieved BAC 0.13%) reported slight impairments in response selection during hangover, but no evidence that response inhibition was influenced by hangover (Opitz et al., 2019). However, a recent systematic review highlighted that hangover-related cognitive impairments tend to be observed in studies following naturalistic alcohol consumption relative to studies that experimentally induced hangover studies (Gunn, Mackus, Griffin, Munafò, & Adams, 2018). As the effects of hangover are positively related to the amount of alcohol consumed (Scholey, Benson, et al., 2019b), it is likely that the contrast between the results of the current study

and previous experimental studies (Zink et al., 2018) may be due to higher levels of alcohol consumption by the participants in our naturalistic design.

Engaging cognitive control processes, such as inhibition, is considered effortful (Gao, Qi, & Zhang, 2017). In the current study, participants reported expending greater mental effort in completing the cognitive tasks, including response inhibition. This increased effort may reflect a reduction in available mental resource whilst experiencing a hangover, possibly due to the processing of attentionally-demanding stimuli such as painful symptoms (Eccleston et al., 1999), or increased fatigue (Boksem et al., 2006; Boksem & Tops, 2008; van der Linden, 2010). As high cognitive load is known to have an impairing effect on inhibitory processes (Lavie et al., 2004), the interference caused by additional processing of hangover symptoms could influence effortful cognitive processes such as inhibition. One recent study found hangover enhances the detrimental effects of cognitive load on cognitive control (Zink et al., 2018), further suggesting that the cognitive resources are reduced during hangover. Together, these results suggest that hangover may adversely affect the ability to engage effortful cognitive processes (e.g. response inhibition) effectively. However, further research is required to corroborate and quantify this effect.

In contrast to studies of acute alcohol intoxication (Adams et al., 2013; M. Field et al., 2004), the current study found no evidence that hangover influences attentional bias towards alcohol-related stimuli. Contrary to our hypothesis, our results provide no support for the hypothesis that participants will show attentional avoidance of alcohol-related stimuli in hangover. We also found no evidence for attentional biases towards alcohol-related stimuli in the hangover state. Therefore, although enhanced attentional bias towards alcohol-related stimuli may contribute toward increased alcohol-seeking behaviours during acute intoxication (M. Field et al., 2010), our results suggest that these do not extend to hangover.

In line with previous research (McKinney & Coyle, 2006), secondary findings from our study showed that participants in the hangover condition experienced

reduced feelings of tranquillity and perceived themselves as being less alert than in the no-hangover condition, indicating that hangover has negative subjective effects. However, although statistically significant and with a large effect size, the absolute differences in alertness were small and therefore may not be meaningful.

The current findings should be interpreted in light of the following strengths and limitations. In our naturalistic design we asked participants to engage in their "typical drinking" behaviour the evening before the hangover session. Our findings support the ecological validity of using a naturalistic design in hangover research, where participants' self-reported alcohol consumption during the hangover condition did not differ from their usual drinking patterns. To resolve discrepancies between naturalistic and experimental hangover designs, future studies could consider incorporating real-time BAC tracking, which would document whether alcohol consumption is indeed higher in the former design. Controlling for individual differences by utilising a within-subject design can also be considered a strength of this study. It is possible that the Visual Dot Probe task was not sensitive to alcohol-related attentional biases as the no-hangover condition also did not register an avoidance or bias towards alcohol-related stimuli. This may be due to the time-period of testing as participants would not usually consume alcohol during the morning. The problems with recording eye-tracking data on the Visual Dot Probe task in the present study may also limit the reliability of our attentional bias findings (Ataya et al., 2012a), where it is recommended that eye-tracking is used alongside behavioural measures (Christiansen et al., 2015). Future studies should seek to replicate the current research with eye-tracking technology to support the current null findings.

To conclude, participants exhibited poorer response inhibition during hangover versus a no-hangover condition. Our results provide no evidence that hangover influences attentional bias toward alcohol-related stimuli (contrary to our hypothesis of attentional avoidance). Secondary findings highlight that participants report lower mood and feel that they have to expend greater mental effort to complete cognitive tasks when experiencing a hangover. Together,

these findings suggest that alcohol hangover is associated with poorer response inhibition and lower mood.

5.6 Additional Analysis

To explore the relationship between hangover severity (as measured by the mAHSS) and alcohol consumption (eBAC), a Bivariate correlational analysis was conducted. There was no evidence that hangover severity was associated with alcohol consumption (r = .063, p = .711). Gender differences were also explored using a 2 (condition) x 2 (gender) repeated measures ANOVA for the commission errors (Go/No-Go) and attentional bias scores (VDP). For both tasks, gender did not influence the results (ps ≥ .391). Furthermore, gender differences for hangover severity (mAHSS) and alcohol consumption (eBAC) were explored using independent t-tests. Analysis indicated no gender differences for hangover severity (p = .443) or alcohol consumption (p = .891).

Results from our additional analysis indicate hangover severity is not related to alcohol consumption. This is in contrast to previous research (e.g., Scholey, Benson, et al., 2019b; Stephens et al., 2017) and surprising given that alcohol hangover is a result of physiological processes responding to heavy alcohol consumption. Additional analysis also indicated no interaction with gender for both the Go/No-Go and VDP tasks. These results are in-line with some previous studies that did not find gender differences in hangover-related impairments (Verster et al., 2003), but in contrast to other studies (Howland et al., 2010). Given the paucity in research exploring gender differences for the cognitive effects of hangover, subsequent studies in this thesis will continue to explore this.

5.7 Commentary Text

The above findings of poorer response inhibition and greater negative affect in hangover have implications for future alcohol-seeking behaviours. However, they also have implications for other behaviours that rely on higher-order thought processes. Although the mechanisms that contribute toward greater negative affect in hangover are unclear, one mechanism that may be influenced

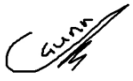
is emotion regulation. Emotion regulation is the ability to control the expression and experience of emotions (Gross, 1998b; Gross et al., 2006). Inhibitory control is an important cognitive process when effectively engaging in the regulation of emotions (Joormann, 2010). Therefore, impairments in response inhibition (above findings) and interference control (Devenney & Verster, 2019; McKinney, Coyle, Penning, et al., 2012) during hangover suggest that emotion regulation may also be influenced. Chapter Six explores this possibility and addresses the third aim of this thesis: To investigate the effects of alcohol hangover on emotion regulation.

The methodological approach utilised in Chapter Five was developed to be as rigorous as possible for a naturalistic approach. It included a screening session, restricted caffeine and nicotine consumption the morning of testing, and required participants to attend the laboratory at the University of Bath for cognitive testing, where extraneous variables (e.g., noise) could be controlled. In addition, attendance was at the same time for each session (i.e. hangover and no-hangover). Although this approach allowed for additional control, elements of the methodological design limited and slowed participant recruitment. For example, when arranging testing sessions it was difficult to have participants attend at the same time for both sessions, which often resulted in participants dropping out or attending their second session after the 7 (+/- 2 day) period. Furthermore, attending three sessions was seen as arduous, particularly as one session was with a hangover, and often 'put off' potential participants. Therefore, the study in Chapter Six built on these limitations by utilising a two-session approach (hangover and no-hangover conditions) and by using a participant harvesting recruitment method. Using this method, participants were approached by the researcher in situ (i.e. cafes, common area of the university). Once information and consent was given, the researcher conducted the first condition according to the participant's present state (hungover, not-hungover). Testing location was also flexible to allow for maximum recruitment opportunities.

Chapter Six: Does Alcohol Hangover Affect Emotion Regulation Capacity? Evidence from a Naturalistic Cross-Over Study Design

Declaration of Authorship

This declaration concerns the article entitled:									
Does Alcohol Hangover Affect Emotion Regulation Capacity? Evidence from a Naturalistic Cross-Over Study Design									
Publication status (tick one)									
Draft manuscript	**X**	**Submitted**		**In review**		**Accepted**		**Published**	
Publication details (reference)									
Copyright status (tick the appropriate statement)									
I hold the copyright for this material	X	Copyright is retained by the publisher, but I have been given permission to replicate the material here							

Candidate's contribution to the paper (provide details, and also indicate as a percentage)	The candidate contributed to / considerably contributed to / predominantly executed the… Formulation of ideas: Predominantly executed Design of methodology: Predominantly executed Experimental work: Predominantly executed Presentation of data in journal format: Considerably contributed		
Statement from Candidate	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature.		
Signed		**Date**	13/02/2020

Does Alcohol Hangover Affect Emotion Regulation Capacity? Evidence from a Naturalistic Cross-Over Study Design

Craig Gunn[1,2], Graeme Fairchild[2], Joris C. Verster[3,4,5], and Sally Adams[1,2]

[1]Addiction and Mental Health Group, Department of Psychology, University of Bath

[2]Department of Psychology, University of Bath

[3]Utrecht Institute for Pharmaceutical Sciences (UIPS), Division of Pharmacology, Utrecht University, 3584CG Utrecht, The Netherlands

[4]Institute for Risk Assessment Sciences (IRAS), Faculty of Veterinary Medicine, Utrecht University, 3584 CM Utrecht, The Netherlands

[5]Centre for Human Psychopharmacology, Swinburne University, Melbourne, VIC 3122, Australia

6.1 Abstract

Previous research has indicated that alcohol hangover can decrease mood and reduce alertness. However, the mechanisms that contribute toward the negative affect experienced during a hangover remain unclear. One possibility is that hangover's effects on emotion regulation underlie these adverse mood effects. Emotion regulation refers to the way individuals control the experience and expression of their emotions. Therefore, the aim of the current study was to investigate the effects of alcohol hangover on emotion regulation. Forty-five non-smoking, healthy participants aged between 18-30 years completed a lab-based emotion regulation task assessing cognitive reappraisal and an emotion regulation questionnaire (State-Difficulties in Emotion Regulation Scale; S-DERS) when hungover (morning following a night of heavy drinking) and under a no-hangover condition in a naturalistic, within-subjects design study. Participants also completed questionnaires measuring hangover severity, mood, sleep quality and sleepiness. Results from the S-DERS indicated poorer overall emotion regulation ($p < .001$, $d = 0.75$), and poorer emotion regulation for the subscales 'Non-Acceptance', 'Modulation', and 'Clarity' ($ps \leq .001$, $ds \geq 0.62$), but not 'Awareness' ($p = .672$, $d = 0.06$) in the hangover relative to the

no-hangover condition. There was no evidence from the task that alcohol hangover impaired emotion regulation ability (ps $\geq$ .214, ds $\leq$ 0.40), but there was a general negative shift in valence ratings of visual stimuli (i.e. all stimuli was viewed more negatively) in the hangover condition (p < .001, d = 1.16). Overall, these results suggest that the ability to regulate emotions in everyday life and emotional reactivity to stimuli may be adversely affected by alcohol hangover, but some emotion regulation strategies (e.g., deliberate cognitive reappraisal) may be unaffected.

6.2 Introduction

Alcohol hangover refers to the combination of mental and physical symptoms, experienced the day after a single episode of heavy drinking, starting when blood alcohol concentration approaches zero (van Schrojenstein Lantman, van de Loo, et al., 2017). Alcohol hangover can impair core cognitive processes, such as short- and long-term memory, sustained attention, and psychomotor speed (Gunn et al., 2018), as well as 'higher-order' executive functions (Heffernan et al., 2019). These impairments may contribute toward the negative effects of hangover on productivity in the workplace, recently estimated to cost the UK economy £1.4 billion per annum (Bhattacharya, 2019). However, alcohol hangover can also negatively influence mood and emotion. Self-report measures have indicated that participants experience increased anxiety (Collins & Chiles, 1978; Marsh et al., 2019; McKinney & Coyle, 2006) and reduced 'tranquillity', which includes items such as happy/sad (Gunn, Verster, & Adams, 2019; McKinney & Coyle, 2006), during a hangover relative to a no-hangover control condition. Furthermore, symptoms of a hangover include negative emotions such as 'anxiety' and 'depression', albeit these are not as commonly reported as other symptoms such as headache or fatigue (van Schrojenstein Lantman, Mackus, et al., 2017). Considered together, these results suggest that negative affect is increased during hangover. Increased negative affect could have a detrimental influence on workplace performance. For example, employees who reported being hungover at work at least once in the past year were more likely to report conflict with colleagues and criticisms from supervisors than those who did not go to work hungover (Ames et al., 1997). However, the cognitive mechanisms that contribute toward negative affect in the hangover state are unclear. One process that may be influenced by hangover and is utilised to maintain emotional equilibrium is emotion regulation.

Emotion regulation is a multidimensional construct that refers to the way people control their experience and expression of emotions (Gross, 1998b; Gross et al., 2006). Emotion regulation involves being aware of one's emotions and why they are experienced, being willing to tolerate temporary emotional distress to achieve one's aims or pursue meaningful activities, and engaging in effortful

cognitive processes to attenuate (or *amplify*) emotional responses to stimuli or situations (Gratz & Roemer, 2004). These cognitive processes include inhibitory control, goal-directed behaviours, and emotion modulation strategies such as cognitive reappraisal or suppression. Cognitive reappraisal can be defined as mentally changing the emotional impact and meaning of potentially emotion-eliciting situations or stimuli. This aspect of emotion regulation has received the majority of attention in the empirical literature (Ochsner et al., 2012). Reappraising the meaning of a stimulus can increase positive affect and reduce negative affect, and frequent use of this emotion regulation strategy is associated with healthier social relationships and greater well-being (Gross & John, 2003). However, reappraisal is a cognitively complex emotion regulation strategy as it utilises a number of executive functions (e.g., inhibiting the initial response and other interfering thoughts, and cognitive switching from the initial appraisal to alternative appraisals (Ochsner & Gross, 2005; Ochsner et al., 2012).

During hangover, cognitive resources that are utilised when engaging in effortful cognitions are reduced (Scholey, Ayre, et al., 2019; Wolff et al., 2016). This may contribute toward impairments in processes needed for efficient emotion regulation during a hangover, such as inhibitory control (Devenney & Verster, 2019; Gunn, Verster, et al., 2019; McKinney, Coyle, Penning, et al., 2012) and executive function (Heffernan et al., 2019; Howland et al., 2010). These results imply that some dimensions of emotion regulation (e.g., deliberate modulation of emotions) could be negatively affected by alcohol hangover, and regulation strategies that are effortful may become less effective. Furthermore, although participants are aware of their current emotions during a hangover (Howland et al., 2010), the social and psychological isolation they feel when hungover could indicate impairments in the ability to regulate emotions (Griffin et al., 2018).

The aim of the current study was therefore to investigate the effect of alcohol hangover on emotion regulation using a widely-used laboratory task that measures cognitive reappraisal. We also used a self-report questionnaire measuring state emotion regulation to investigate the effect of hangover on

additional dimensions of emotion regulation and assess emotion regulation in real-life situations. We hypothesised that participants would show impaired emotion regulation whilst hungover compared to a no-hangover control. We also hypothesised that engaging in deliberate cognitive reappraisal would be perceived as more effortful during hangover compared to a no-hangover control, and that emotion regulation would negatively correlate with hangover severity.

6.3 Methods

6.3.1 Participants

As with the study presented in Chapter Five, an a-priori power analysis, conducted using G-Power and an effect size of $\eta_p^2 = 0.172$ (McKinney et al. 2012), revealed 34 participants were required. As the previous study (Chapter Five) had a high attrition rate (37%), this study aimed to recruit 44 participants (22 males, 22 females).

Participants were recruited via the 'harvesting' method (Crandall et al., 1997). Individuals were approached on campus and in popular general public areas (e.g., cafes) by the researcher and asked if they would like to participate in the study. Participants (n = 45, 24 male, 21 female) consumed $\geq$ 6 (female) or ≥ 8 (male) units of alcohol on a typical night of heavy drinking, were non-smokers aged between 18 – 30 years, and reported themselves as being in general good mental and physical health. To exclude the potential confound of hangover resistance, participants were required to have experienced a hangover in the past month. Participants were excluded if they were pregnant/breast-feeding, taking medication or using recreational drugs, reported consuming > 400mg caffeine per day (equivalent to 4 large coffees), had a current or past personal or family history of drug dependency, or had a diagnosed sleep disorder. Participants consumed an average of 13.9 (SD = 5.8; range = 6 – 26.5) units of alcohol, reaching an estimated Blood Alcohol Concentration (eBAC) of 0.15% (SD = 0.07; range = 0.03 – 0.32), on the night before the hangover testing session. Some participants (n = 4) consumed small amounts of alcohol the night before the no-hangover condition despite

instructions to refrain from alcohol consumption at least 24-hours prior to testing and were therefore excluded from analysis. Upon completion of both conditions, participants were paid £10 and received a full debrief. The University of Bath Psychology Research Ethics Committee approved this research, ethics code: 18-086.

6.3.2 Design

The study was an experimental 'naturalistic' design, with a within-subjects factor of condition (hangover, no-hangover). Hangover researchers have argued that the naturalistic design is preferred to the experimental approach when exploring the real-life cognitive of alcohol hangover (Verster et al., 2019). Participants refrained from alcohol consumption for at least 24 hours prior to testing in the no-hangover condition, whilst the hangover condition took place the morning following an evening of heavy alcohol consumption. Both sessions took place in a similar location (e.g. lab, café, etc.) and time to when participants completed the first session. Participants completed the hangover condition first, or the no-hangover condition first depending on the state that they were in when first recruited. Therefore no formal randomisation was conducted, however, order was counterbalanced during recruitment so that approximately 50% of participants completed the no-hangover condition first.

6.3.3 Materials and Measures

Participants reported alcohol consumption for the previous night and eBAC was calculated using the Widmark formula (National Highway Traffic Safety Administration, 1994). Participants completed a 1-item hangover severity scale, the modified Alcohol Hangover Severity Scale (mAHSS; Hogewoning *et al.*, 2016), the Groningen Sleep Quality Scale (Mulder-Hajonides van der Meulen, Wijnberg, Hollander, De Diana, 1980), and the Karolinska Sleepiness Scale (Åkerstedt & Gillberg, 1990). Participants also completed a VAS mood scale (Bond & Lader, 1974) comprising of the two factors 'tranquillity' and 'alertness' (Herbert et al., 1976), reported any events from the previous night that may affect their emotions (e.g., argument with partner), and completed a rating scale of mental effort (Zijlstra & Van Doorn, 1985).

The State-Difficulties in Emotion Regulation Scale (S-DERS) was used to measure state changes in emotion regulation (Lavender et al., 2015). The S-DERS is a 21-item questionnaire that provides a total score and four subscale scores that reflect different dimensions of emotion regulation. The 'Non-Acceptance' subscale is comprised of six items that reflect a negative response to current emotions (e.g., 'I feel ashamed with myself for feeling this way'). The 'Modulate' subscale is comprised of seven items that reflect difficulties with modulating emotional and behavioural response (e.g., 'I am having difficulty controlling my behaviours'). The 'Awareness' subscale is comprised of five items that reflect a limited attention to and awareness of current emotions (e.g., 'I am acknowledging my emotions'), and the subscale 'Clarity' is comprised of two items reflecting problems identifying current emotions (e.g., 'I am confused about how I feel'). Participants were asked to indicate how much each item applied to their emotions at that moment in time (1 = not at all, 5 = completely).

Participants completed an emotion regulation task assessing cognitive reappraisal (McRae et al., 2012; Ochsner & Gross, 2005; Urry, 2006). Participants viewed images from the International Affective Picture System (IAPS; Peter J. Lang, Greenwald, Bradley, & Hamm, 1993), which depicted either positive or negative emotional content (e.g., puppies or a dead body), or were neutral images (e.g., a chair). IAPS numbers are given in the Appendix 1. Prior to an image, participants were instructed to either up-regulate their emotions ('INCREASE'), down-regulate their emotions ('DECREASE'), or look at the image without initiating any emotion regulation strategy ('LOOK'). Decrease instructions were given for negative images, increase instructions for positive, and look instructions for negative, positive, and neutral images. There were therefore five trial types: Decrease-Negative, Look-Negative, Increase-Positive, Look-Positive, and Look-Neutral.

Prior to the task, participants were given suggestions of ways in which they could regulate emotions (e.g., "Imagine it is just an image from a movie") and completed 10 practice trials, after which, participants described their regulation

techniques and corrective instructions were given if necessary. Trials began with an instruction (1 second), followed by a positive, negative, or neutral image (5 seconds) with the instruction below. Images were presented in a random order. After the presentation of the image, participants rated their emotions on two dimensions; Arousal (level of excitement in response to stimuli) and Valence (pleasantness of stimuli), using the Self-Assessment Manikin (SAM; Lang, 1980). The SAM is a rating system using graphical figures that provides a quick, non-verbal method of quantifying Valence (1 = left hand figure (unhappy manikin), and 9 = right hand figure (happy manikin)) and Arousal responses (1 = left hand figure (asleep), and 9 = right hand figure (heart beating fast)) to stimuli on a 9-point scale. There were 100 experimental trials (20 for each trial type) presented in a single block, with each image shown once (110 images including practice trials). To ensure that the comparison of affective ratings in the regulate and look conditions was valid, the images were also matched for Valence and Arousal scores across instruction-stimuli pairs (e.g., Look-Negative and Decrease-Negative). A schematic representation of the task is presented in Figure 6.1.

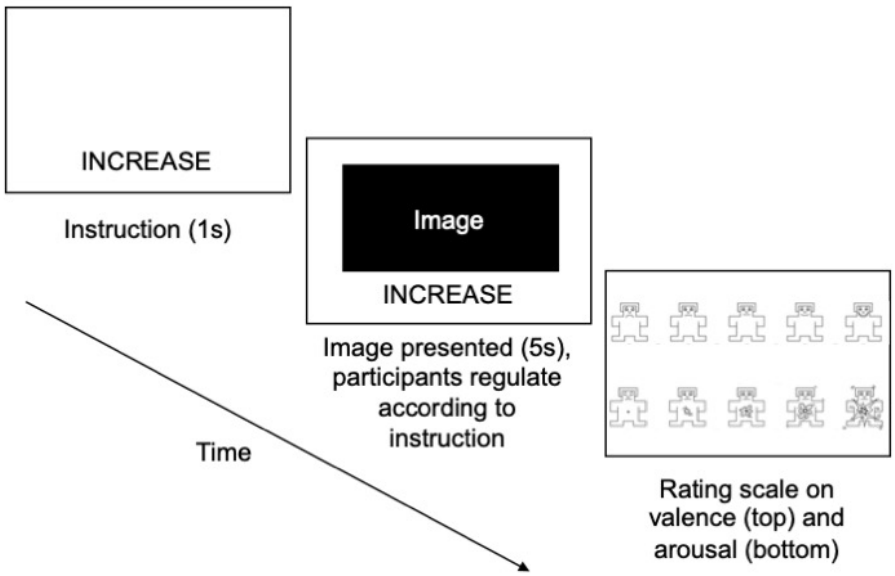


Figure 6.1. Schematic representation of the emotion regulation task. Participants were presented with an instruction (INCREASE, DECREASE, or LOOK) for 1 second before an image (Negative, Positive, or Neutral) was presented for 5 seconds. During this time participants regulated their emotions according to the instruction or simply viewed the images (in the 'LOOK' condition). Participants then rated their emotions in terms of Valence and Arousal using the Self-Assessment Manikin (P J Lang, 1980).

6.3.4 Procedure

Participants were given information about the study when they were approached and invited to take part and they provided written informed consent before testing began. Participants reported on their previous night alcohol consumption, caffeine consumption, and potential emotional events that may have occurred prior to testing. Participants were breathalysed and completed the sleep, hangover, mood, and emotion regulation questionnaires before completing the cognitive reappraisal task. This was followed by completion of the rating scale for mental effort. The second testing session was then arranged for at least 36 hours after the first to prevent crossover effects.

6.3.5 Statistical Analysis

Four subjects were excluded from the statistical analysis as they reported consuming alcohol on the alcohol-free control day. Outliers were removed from data if they were > 1.5*inter-quartile range and > 2 SD from the mean. Statistical analysis was performed using SPSS (version 24) and where data were non-normally distributed, bootstrapping of 5000 samples was performed (A. P. Field, 2018). Where multiple comparisons were conducted, a Bonferroni's correction was applied. As acute intoxication effects on cognition have been observed at BAC > 0.02% (Holloway, 1994), the statistical analysis were also conducted excluding participants with a BAC > 0.02% at testing.

6.4 Results

6.4.1 Effects of Hangover on Emotion Regulation

As the S-DERS is a measure of emotion dysregulation, higher scores indicate greater emotion dysregulation ('poorer emotion regulation'). A paired sample t-test indicated that total S-DERS scores were greater ($t(41) = 4.863$, $p < .001$, $d = 0.75$) in the hangover condition than the no-hangover condition. The subscales 'Non-Acceptance', 'Modulation', 'Awareness', and 'Clarity' were calculated as per (Lavender et al., 2015) and compared between conditions using a series of paired-sample t-tests (Bonferroni corrected alpha 0.007). As with total scores, higher scores in each subscale indicates poorer emotion

regulation. Non-Acceptance ($t(37) = 5.244$, $p = .001$, $d = 0.85$), Modulation ($t(40) = 5.465$, $p < .001$, $d = 0.85$), and Clarity scores ($t(40) = 3.974$, $p = .001$, $d = 0.62$) were all greater in the hangover than the no-hangover control condition. However, awareness scores did not differ between conditions ($p = .672$. Mean and SD scores for each factor are presented in Table 1.

Table 1. *Means, standard deviations, and group comparisons for each subjective variable*

Variable	Hangover		No-Hangover		*P*	*Effect size*
	M	SD	M	SD		
State Emotion Regulation questionnaire (S-DERS)[a]						
Total	39.64	10.92	32.62	7.20	< .001	*d* = 0.75
Non-Acceptance	9.08	2.94	7.66	2.45	.001	*d* = 0.85
Modulation	11.78	4.89	8.44	2.63	< .001	*d* = 0.85
Awareness	13.85	4.16	13.61	4.44	.694	*d* = 0.06
Clarity	3.68	1.79	2.66	1.15	.001	*d* = 0.62
Mood						
Tranquillity Factor	44.16	4.72	46.92	4.92	.016[b]	*d* = 0.39
Alertness Factor	47.90	4.92	56.26	4.83	< .001	*d* = 1.53
Hangover Severity						
mAHSS	2.95	1.57	0.23	0.29	< .001	*d* = 1.96
1-item Hangover Scale	4.71	1.92	0.14	0.93	< .001	*d* = 2.33
Sleep						
GSQS (Quality)[a]	6.14	1.52	5.57	1.21	.070	*d* = 0.29
KSS (Sleepiness)[a]	6.68	1.53	3.15	1.27	< .001	*d* = 2.27
Mental Effort						
RSME	71.36	26.90	44.36	21.28	< .001	*d* = 1.02

Note: M, mean; SD, standard deviation; S-DERS, State-difficulties in emotion regulation scale; mAHSS, modified Alcohol Hangover Severity Scale; GSQS, Groningen Sleep Quality Scale; KSS, Karolinska Sleepiness Scale; RSME, Rating Scale of Mental Effort. [a] higher scores indicate poorer performance.

6.4.2 Emotion Regulation Task

Regulation scores for negative stimuli were calculated by subtracting affect rating scores on Look-Negative trials from Decrease-Negative trials, and regulation scores for positive stimuli were calculated by subtracting affect rating scores on Look-Positive trials from Increase-Positive trials. In both cases, a higher score indicates greater emotion regulation. We investigated the effect of hangover on regulation scores of Valence and Arousal using a 2 (Condition: Hangover, No-Hangover) x 2 (Stimulus type: Negative, Positive) repeated measures ANOVA. For Valence scores there were no main effects or interactions ($ps \geq .214$), and for Arousal there was a main effect of stimulus type only ($F(1, 41) = 27.296$, $p < .001$, $d = 1.63$), whereby regulation scores for Arousal were lower for negative stimuli than positive stimuli.

Although not part of our original analysis plan, we found there were differences between the hangover and no-hangover conditions in overall affect ratings. We therefore explored the influence of hangover on affective ratings of Valence and Arousal using a 2 (Condition) x 5 (Instruction-Stimuli pair) repeated measures ANOVA. For raw valence scores (rather than the difference scores which specifically index emotion regulation), there was a main effect of Condition (F(1, 35) = 11.926, p = .001, d = 1.16), whereby participants rated the images as being lower in Valence overall (i.e., less positive) in the hangover condition than the no-hangover condition. Means and SD scores for the emotion regulation task are presented in Table 2 and results are presented graphically in Figure 6.2.

Table 2. *Means, standard deviations, and group comparisons for the emotion regulation task*

Variable	Hangover		No-Hangover		*P*	*Effect size*
	M	SD	M	SD		
Emotion Regulation Task:						
Regulation Scores: Valence	0.35	0.38	0.42	0.40	.214	d = 0.40
Regulation Scores: Arousal	-0.05	0.41	-0.12	0.40	.609	d = 0.16
Affect Ratings: Valence	4.90	0.33	5.07	0.28	< .001	d = 1.16
Affect Ratings: Arousal	3.93	1.51	3.80	1.43	.168	d = 0.47

Note: M, mean; SD, standard deviation; Regulation scores were calculated by subtracting Look trials from Regulate trials in the emotion regulation task.

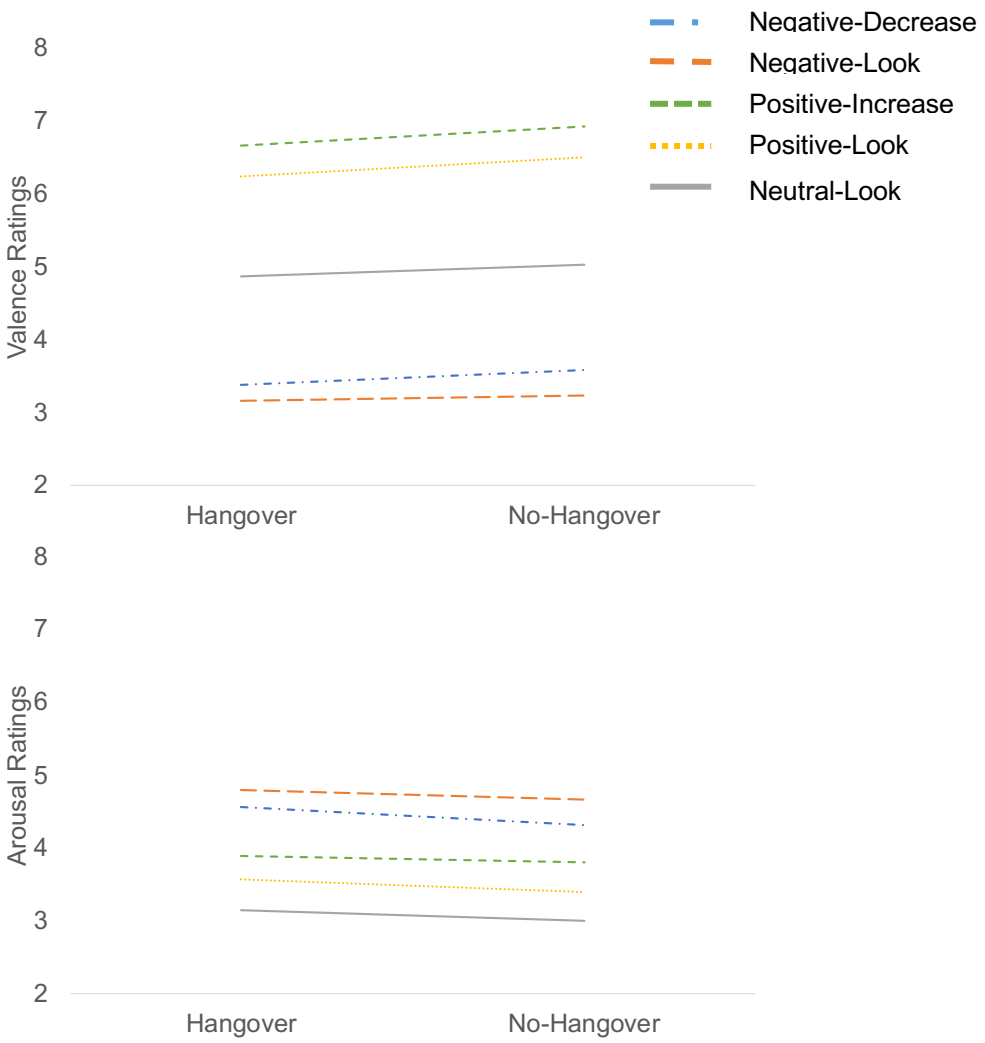


Figure 6.2. Graphical representation of mean ratings for stimuli on the emotion regulation task. Participants rated the visual stimuli as lower in Valence overall in the hangover versus the no-hangover condition (top panel). There were also clear effects of emotion regulation instruction, with positive stimuli being rated as higher in Valence in the Positive-Increase compared to the Positive-Look condition, and lower in Valence for the Negative-Look than the Negative-Decrease instructions. There was no evidence that condition influenced ratings of Arousal (bottom panel), but there was a main effect of stimuli-instruction pairs, which indicated that stimuli in the Neutral-Look condition were rated as being lowest in Arousal and those in the Negative-Look were highest in Arousal.

6.4.3 Subjective Questionnaires

The two factors 'tranquillity' and 'alertness' were calculated from VAS mood questionnaire scores as per (Herbert et al., 1976) and analysed separately. A paired sample t-test indicated that tranquillity scores were reduced ($t(41) = 2.502$, $p = .016$, $d = 0.39$) in the hangover compared to the no-hangover

condition. Alertness scores were also reduced ($t(39) = 9.652$, $p < .001$, $d = 1.53$) in the hangover compared to the no-hangover condition.

Separate paired sample t-tests indicated sleepiness scores were greater ($t(39) = 14.362$, $p < .001$, d = 2.27) in the hangover condition than the no-hangover condition, but Groningen Sleep Quality Scale scores differed at a trend level only ($p = .07$). A paired-samples t-test also indicated that RSME scores were greater ($t(41) = 6.616$, $p < .001$, $d = 1.02$) in the hangover than no-hangover condition.

6.4.4 Correlational Analysis

To address our third hypothesis, we performed Bivariate correlations testing for relationships between hangover severity (as measured by the mAHSS) and emotion regulation (with a Bonferroni adjusted alpha of 0.007). These showed that hangover severity was strongly positively correlated with emotion dysregulation, as measured with the S-DERS ($r = .651$, $p < .001$). This was also the case for the S-DERS subscales Modulation ($r = .662$, $p < .001$) and Clarity ($r = .609$, $p < .001$), but not Non-Acceptance ($r = .359$, $p = .025$) or Awareness ($r = .235$, $p = .139$). However, there were no significant associations between hangover severity and regulation for positive or negative stimuli in the emotion regulation task ($ps \geq .329$).

6.4.5 Results when excluding subjects with a BAC > 0.02%

The results remained the same when excluding 5 participants with a BAC > 0.02% at testing, with the exception of the hangover effects on tranquillity which were reduced to trend significance ($p = .08$).

6.5 Discussion

In line with our first hypothesis, perceived emotion regulation was impaired in the hangover compared to no-hangover condition. This was reflected by greater total emotion dysregulation scores on the S-DERS – a questionnaire covering a variety of emotion regulation strategies used in day-to-day life. When analysing

each subscale of the S-DERS, participants had a greater negative response to their emotional state (Non-Acceptance), had greater difficulties with emotional and behavioural responses (Modulation), and had greater problems identifying emotional states (Clarity) when hungover. However, there was no difference in awareness of current emotional state (the amount of attention given to emotions) when hungover compared to a no-hangover control. In contrast, there was no difference between conditions in performance on an objective measure of emotion regulation ability (differences in affective ratings between regulate and look trials during the emotion regulation task). However, the participants did rate emotional stimuli as more negative in Valence in the hangover compared to the no-hangover condition – and this was true for both the Look and Regulate trials of the emotion regulation task. Therefore, these results reflect a tonic effect on emotional reactivity (as even positive stimuli were evaluated as being less positive) rather than a specific effect on *emotion regulation* or regulation of negative affect. Results from our correlational analyses lent partial support to our hypothesis, where hangover severity was positively associated with emotion dysregulation, but there were no associations between hangover severity and regulatory capacity in the emotion regulation task.

Although results from the self-report questionnaire measure indicated poorer emotion regulation during hangover, the results of the cognitive task indicated that cognitive reappraisal (a deliberate emotion regulation strategy) was unaffected by hangover. However, the design of the cognitive task, which instructed participants to engage in cognitive reappraisal as part of the study, may have prevented effects being observed. As cognitive reappraisal is cognitively demanding (Urry, 2006; Urry et al., 2009), it is possible that fewer available cognitive resources during a hangover (Scholey, Ayre, et al., 2019; Wolff et al., 2016) would shift motivation away from effortful processes, and participants would be less likely to spontaneously use cognitive reappraisal strategies in real-life. Our findings of greater perceived difficulties with modulating emotions and behaviour when hungover compared to a no-hangover control may reflect a difficulty to engage in cognitively demanding regulation strategies. This is further supported by our finding of greater perceived mental effort to complete the lab-based task, as they may be less

motivated to engage in effortful emotion regulation strategies – the efficiency of such processes may be reduced, even while the effectiveness is unaffected. Therefore, future research could use experience-sampling methods to investigate which emotion regulation strategies are adopted in hangover, if these are different to those which are regularly used, and how effective these strategies are when used spontaneously (in response to frustrating or rewarding events experienced in everyday life).

In line with our a-priori hypothesis, our results highlight a positive association between hangover severity and emotion dysregulation. Although underlying mechanisms cannot be established in the current study, it is possible that symptoms, such as headache (Attridge et al., 2017), consume cognitive resources leaving fewer available to allocate to effective emotion regulation. Fatigue can also impair the ability to effectively allocate cognitive resources during goal-directed behaviours (Boksem et al., 2005). Alternatively, engaging in emotion regulation can reduce cognitive resource (Schmeichel, 2007), leaving fewer available to process symptoms of a hangover (e.g., fewer resources allocated to reducing nausea). Further research is warranted to investigate the underlying mechanisms of the relationship between hangover severity and emotion regulation.

The current findings should be viewed in light of the following strengths and limitations. The within-subject naturalistic design of the current study should be viewed as a strength as each participant serves as their own control. However, the participant harvesting method design could be seen as a limitation as participants were tested in potentially noisy environments (e.g., cafés). Furthermore, given a reasonable effect size was observed, the current study may have been underpowered to observe effects in the lab-based emotion regulation task.

Emotion regulation is important for everyday behaviours, such as maintaining relationships and engaging in meaningful goal-directed activities (Gross, 2015). Our results suggest that hangover may negatively influence the ability to

effectively regulate emotions in everyday life. As emotion regulation is positively associated with the quality of interpersonal interactions (Lopes, Salovey, Côté, & Beers, 2005), poor emotion regulation and low mood in hangover may contribute toward problems in workplace roles that require interaction with others, such as during meetings or whilst teaching (Buvik, Moan, & Halkjelsvik, 2018).

In conclusion, our results highlight poorer emotion regulation in hangover as assessed using a self-report measure, but not a lab-based task measuring a core aspect of emotion regulation (cognitive reappraisal). However, results from the cognitive task did suggest that there is a general negative shift in the emotional appraisal of visual stimuli during hangover, suggesting hangover caused participants to react more negatively to stimuli. This finding merits further investigation and needs to be replicated in larger samples, alongside different aspects of emotion regulation (e.g., emotional acceptance) or other emotion regulation strategies (e.g., suppression).

6.6 Additional Analysis

The relationship between hangover severity (as measured by mAHSS) and alcohol consumption (eBAC), and gender differences in the effects of hangover on emotion regulation (S-DERS and emotion regulation task) were explored. Bivariate correlational analysis indicated an association between hangover severity and alcohol consumption (eBAC; r = .407, p = .006, 95%CI [0.17 – 0.61]). A 2 (condition) x 2 (gender) repeated measures ANOVA for S-DERS total scores indicated a main effect of condition only ($F(1, 43) = 16.831$, $p < .001$, $d = 1.25$), whereby scores were greater in the hangover relative to the no-hangover condition. Gender differences in the emotion regulation task were explored using 2 (condition) x 2 (stimuli) x 2 (gender) repeated measures ANOVAs for valence and arousal regulation scores in the emotion regulation task. For valence scores, results indicated no main or interaction effects (ps ≥ .392), and for arousal scores there was a main effect of stimuli only ($F(1, 43) = 33.311$, $p < .001$, $d = 1.76$), whereby regulation was greater for positive (M = 0.35, SD = 0.50) than negative stimuli (M = -0.35, SD = 0.58). Furthermore,

independent t-tests indicated no gender differences for hangover severity (p = .974) or alcohol consumption (p = .687).

In-line with previous studies (Scholey, Benson, et al., 2019b; Stephens et al., 2017), results from the additional analysis indicate that there was an association between hangover severity and alcohol consumption. However, these results are in contrast to the study presented in Chapter Five which indicated no relationship. Furthermore, results indicated there were no gender differences in the effect of hangover on emotion regulation. This was the case for both perceived emotion regulation (as measured by the S-DERS) and cognitive reappraisal (as measured by the emotion regulation task). It should be noted that there was a main effect of stimuli for arousal scores in the emotion regulation task. As participants were up-regulating emotions for positive stimuli (i.e., increasing intensity of the emotions experienced) and down-regulating emotions for negative stimuli (i.e., reducing the intensity of emotions experienced), this effect suggests that participants were engaged with the task and regulated their emotions effectively.

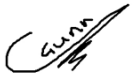
6.7 Commentary Text

Results from the experimental studies so far indicate that cognitive processes that rely on executive functions are impaired in hangover, although the effective completion of some tasks (e.g., cognitive reappraisal) may be achievable with increased mental effort. Furthermore, studies have recently indicated that hangover could impair other higher-order cognitions, such as prospective memory (Heffernan, 2018; Heffernan et al., 2019), verbal semantic memory (Heffernan et al., 2019), and reward learning (Howse et al., 2018). Together, these findings suggest that executive function processes are negatively influenced by hangover. However, few studies have investigated the influence on 'core' components of executive functions suggested by the unity/diversity model – attentional switching, updating information in working memory, and goal maintenance (Friedman & Miyake, 2017). Therefore, the following chapter will present the final study of this thesis that aimed to investigate the effect of hangover on executive functions (switching, updating, and goal-maintenance).

The methodological design of this study (Chapter Six) worked well for recruitment, and there was lower attrition compared with the study in Chapter Five (22% and 37% attrition respectively). However, as participants who were approached by the researcher tended to book a session, rather than conducting the study there and then, the participant harvesting method was dropped from the design of the final study (Chapter Seven). Therefore, the following study adopted broadly the same methodological approach as Chapter Six, but did not utilise the participant harvesting method.

Chapter Seven: The Effects of Alcohol Hangover on Executive Functions

Declaration of Authorship

This declaration concerns the article entitled:			
The Effects of Alcohol Hangover on Executive Functions			
Publication status (tick one) **Draft manuscript** [ ] **Submitted** [ ] **In review** [ ] **Accepted** [ ] **Published** [X]			
Publication details (reference)			
Copyright status (tick the appropriate statement) I hold the copyright for this material [X] Copyright is retained by the publisher, but I have been given permission to replicate the material here [ ]			
Candidate's contribution to the paper (provide details, and also indicate as a percentage)	The candidate contributed to / considerably contributed to / predominantly executed the… Formulation of ideas: Predominantly executed Design of methodology: Predominantly executed Experimental work: Predominantly executed Presentation of data in journal format: Considerably contributed		
Statement from Candidate	This paper reports on original research I conducted during the period of my Higher Degree by Research candidature.		
Signed		**Date**	13/02/2020

The Effects of Alcohol Hangover on Executive Functions

Craig Gunn [1,2], Graeme Fairchild [2], Joris C. Verster [3,4,5], and Sally Adams [1,2]

[1] Addiction and Mental Health Group, Department of Psychology, University of Bath;
[2] Department of Psychology, University of Bath;
[3] Division of Pharmacology, Utrecht University, 3584CG Utrecht, The Netherlands;
[4] Institute for Risk Assessment Sciences (IRAS), Utrecht University, 3584CM Utrecht, The Netherlands
[5] Centre for Human Psychopharmacology, Swinburne University, Melbourne, VIC 3122, Australia
* Correspondence: craig.a.gunn@gmail.com, S.Adams@bath.ac.uk

7.1 Abstract

Recent research has suggested that processes reliant on executive functions are impaired by alcohol hangover, yet few studies have investigated the effect of hangover on core executive function processes. Therefore, the current study investigated the effect of hangover on the three core components of the unity/diversity model of executive functions: the ability to switch attention, update information in working memory, and maintain goals. Thirty-five 18-30 year old, non-smoking individuals who reported experiencing a hangover at least once in the previous month participated in this study. They completed tasks measuring switching (number-switching task), updating (n-back task), and goal maintenance (AX-CPT) whilst experiencing a hangover and without a hangover in a 'naturalistic' within-subjects, crossover design. Participants made more errors in the switching task (p = .019), more errors in the 1- ($p < .001$) and 2-back ($p < .001$) versions of the n-back, and more errors in the AX-CPT (p = .007) tasks when experiencing a hangover, compared to the no-hangover condition. These results suggest that alcohol hangover impairs core executive function processes that are important for everyday behaviours such as decision-making, planning, and mental flexibility.

Keywords: Alcohol; Hangover; Executive Functions; Working Memory; Cognition

7.2 Introduction

Alcohol hangover is a combination of mental and physical symptoms, experienced the day after a single episode of heavy drinking when blood alcohol concentration (BAC) approaches zero (van Schrojenstein Lantman, van

de Loo, et al., 2017). It is the most common negative consequence of heavy drinking and can impair cognitive processes, such as sustained attention, memory, and psychomotor skills (Gunn et al., 2018; McGee & Kypri, 2004). However, relatively few studies have investigated the effect of alcohol hangover on core components of executive functions.

Executive functions are higher-order cognitive processes used in everyday behaviours such as decision-making, mental flexibility, and planning. Recent studies have indicated that executive functions may be negatively influenced by alcohol hangover. Studies have suggested that performance on tasks of interference control (Devenney et al., 2019; McKinney, Coyle, Penning, et al., 2012) and response inhibition (Gunn, Verster, et al., 2019) is impaired when subjects are experiencing a hangover, suggesting poorer inhibitory control – which may negatively influence decisions around subsequent alcohol use (Noël et al., 2007) and emotion regulation (Schmeichel et al., 2008) during the hungover state. Furthermore, findings showing poorer spatial working memory (Devenney et al., 2019), reward learning (Howse et al., 2018), prospective memory (Heffernan, 2018; Heffernan et al., 2019), semantic verbal fluency (Heffernan et al., 2019) and performance on backward visual span tasks (Howland et al., 2010) indicate that executive functions are impaired whilst experiencing a hangover. A recent report by the Institute of Alcohol Studies suggested that the cost of reduced productivity at work during a hangover could be as high as £1.4 billion per annum in the UK (Bhattacharya, 2019). As effective workplace performance relies on an individual's ability to make decisions, organise tasks, and plan, detrimental effects of hangover on executive functions may contribute toward these costs. Therefore, it is important to understand how these processes may be influenced the morning after a night of heavy alcohol consumption, i.e. during hangover.

Executive functions are utilised when behaviours need to be controlled (rather than when they are 'automatic'), when cognitive processes are combined, or when individuals need to switch attention between tasks (Husain, 2017). The unity/diversity model conceptualises executive functions as being comprised of

two core components, alongside a single common factor that is utilised in all executive function tasks (Friedman & Miyake, 2017). The two components represent the ability to switch attention from one task/mental set to another (switching), and the ability to update information within working memory (updating). The common factor of the unity/diversity model represents the ability to maintain and manage goals in order to effectively complete tasks (goal maintenance). All executive function tasks utilise aspects of these core components. As hangover-related impairments have been observed in higher-order cognitive processes, such as prospective memory (Heffernan et al., 2019), it is possible that hangover influences these core components of executive function.

Attentional switching requires allocation of attentional resources to effectively switch from one task or mental set to another (Lépine, Bernardin, & Barrouillet, 2005). Recent studies have indicated that hangover may be a state in which individuals experience high cognitive load (Zink et al., 2018) and thus have fewer available resources to switch attention (Scholey, Ayre, et al., 2019; Wolff et al., 2016). When available cognitive resources are low, completion of executive function tasks becomes ineffective or inefficient (Eysenck et al., 2007; Lavie & Dalton, 2014; Lavie et al., 2004). Factors associated with heavy alcohol consumption, such as a reduction in glutamatergic and an increase in GABAergic, dopaminergic, and serotonergic neurotransmission may also influence attentional switching (Goldstein & Volkow, 2011; Stock & Beste, 2014). In hangover, dopaminergic neurotransmission may be reduced and noradrenaline may be elevated (Howse et al., 2018; Maki et al., 1998), suggesting switching could become impaired. Furthermore, studies have highlighted that fatigue (which is one of the most commonly reported symptoms of a hangover (Penning et al., 2012a) can lead to impairments in switching (Linden et al., 2003).

Thus far, studies investigating attentional switching in individuals experiencing a hangover have yielded mixed results. One study induced hangover experimentally (Wolff et al., 2016) and reported no effect on switch costs –

reflecting the additional time needed to switch attention to the new rule set. However, experimental hangover manipulations involve administering lower doses of alcohol than are typically consumed when drinking in everyday life (Verster, de Klerk, et al., 2014), which could influence the effects of a hangover (Scholey, Benson, et al., 2019b). Two naturalistic studies, which involve assessing the impact of hangovers experienced following real-life drinking, have investigated the effects of hangover on perseveration errors – erroneous responses made according to the previously correct rule or set, reflecting a switching failure. One reported that hangover did not influence switching performance in a non-student sample (Devenney et al., 2019), whereas another study using a student sample indicated poorer switching accuracy when experiencing a hangover compared to a control condition (Devenney & Verster, 2019). It is possible that hungover individuals attempt to maintain performance on switching tasks by either sacrificing accuracy to maintain the speed of their responses, or by sacrificing speed to maintain accuracy (i.e., a 'speed-accuracy trade-off').

To our knowledge, no studies have investigated the effects of alcohol hangover on updating and goal maintenance; however, there are indications that both processes could be negatively affected by hangover. Goal maintenance is an important process utilised to complete all executive function tasks (Friedman & Miyake, 2017). For example, an individual completing a task at work (e.g., writing a report) would need to keep their overall goal in mind whilst planning, organizing, and making decisions about the individual task subcomponents. If goal maintenance is impaired, individuals may be less effective or efficient at completing complex tasks with multiple subcomponents. As previously mentioned, studies have indicated impairments in working memory performance, prospective memory, and semantic verbal fluency during hangover – all tasks requiring executive functions (Devenney et al., 2019; Heffernan, 2018; Heffernan et al., 2019; Howland et al., 2010). Therefore, it is possible that a common factor underlying hangover-related impairments in each of these tasks is a deficit in the ability to maintain goals. Inhibitory control is also impaired when experiencing a hangover (Devenney et al., 2019; Gunn, Verster, et al., 2019; McKinney, Coyle, Penning, et al., 2012) and is a key part of goal

maintenance (Friedman & Miyake, 2017), further suggesting goal maintenance could be influenced by hangover. In addition, reduced cognitive resource in hangover may influence goal maintenance by biasing individuals towards reacting to external events (i.e., bottom up stimulus-driven processing) rather than proactive control of one's actions (i.e., actively sustaining goal representations through top-down processing) (Scholey, Ayre, et al., 2019; Speer, Jacoby, & Braver, 2003). The AX Continuous Performance Task (AX-CPT) can be used to assess goal maintenance and can differentiate between proactive and reactive control (Gonthier, Macnamara, Chow, Conway, & Braver, 2016).

The process of updating information in working memory can become impaired by high cognitive load and when there is a reduction in available cognitive resource (Botto, Basso, Ferrari, & Palladino, 2014). As previously mentioned, cognitive resources may be reduced in hangover (Scholey, Ayre, et al., 2019; Wolff et al., 2016), which could negatively affect the ability to update information in working memory. Furthermore, a study of the cognitive effects of pain indicate that headache can impair performances on tasks measuring updating (Moore et al., 2013). By using an n-back task with conditions that vary in difficulty, studies have also demonstrated that cognitive load selectively influenced the disrupting effect of pain on updating (Moore, Eccleston, & Keogh, 2017). In addition, studies have indicated that updating can become impaired following sleep deprivation (Martínez-Cancino et al., 2015). As headache is a 'core' hangover symptom (van Schrojenstein Lantman, van de Loo, et al., 2017), and individuals often fail to get enough sleep because they choose to continue drinking (Verster, 2008), updating ability may also be compromised by hangover. To assess these effects we used an n-back working memory task with two conditions that vary in difficulty (1-back and 2-back).

The current study aimed to investigate the effects of alcohol hangover on all three of the core components of the unity/diversity model of executive functions: switching, updating, and goal maintenance. Specifically, we hypothesised that participants experiencing a hangover would show impairments in (1) switching,

(2) updating, and (3) goal maintenance compared to the no-hangover control condition. We also hypothesised that participants would adopt a more reactive control style on the AX-CPT task in the hangover condition compared to the no-hangover condition and that the magnitude of impairments in goal maintenance, updating, and switching abilities would be positively associated with hangover severity. As effective completion of executive function tasks may be related to self-efficacy (the belief we have in our own abilities (Chow, Hui, & Lau, 2015)), and self-efficacy is lower when individuals are experiencing a hangover (Finnigan et al., 2005; Howland et al., 2010), we also explored the relationship between self-efficacy and task performance. We hypothesised that performance in goal maintenance, updating, and switching tasks would be positively associated with self-efficacy to complete these tasks.

7.3 Materials and Methods

7.3.1 Participants

As with the previous studies in this thesis, an a-priori power analysis was conducted using G-Power and an effect size of $\eta_p^2 = 0.172$ (McKinney et al. 2012), revealing 34 participants were required. As the previous study (Chapter Six) had success in reducing attrition relative to the study presented in Chapter Five (22% versus 37%), the current study aimed to recruit 40 participants (20 males, 20 females).

Thirty-eight participants were recruited from a student population by poster/flyer and digital advertisements, the University of Bath research participation scheme, word of mouth, and direct approach by the researcher. Inclusion criteria required participants to consume at least 6 (female) or 8 (male) units of alcohol in a typical heavy drinking session, to be aged between 18 – 30 years old, to be non-smokers and in general good mental and physical health. To exclude the potential confound of hangover-resistance, only participants who reported experiencing a hangover in the past month were recruited. Participants who were pregnant/breast-feeding, taking medication or recreational drugs, consuming > 400mg caffeine per day, had a current or past personal or family history of drug dependency, or had a diagnosed sleep disorder were excluded.

Three participants withdrew before completing both conditions, thus 35 participants (14 male, 21 female) completed the study. The University of Bath Psychology research ethics committee approved this research, ethics code: 18-328.

7.3.2 Design

An experimental 'naturalistic' design, with one within-subjects factor of condition (hangover, no-hangover) was used. The naturalistic design is the preferred method when one is interested in examining the real-life cognitive effects of alcohol hangover, and it has been successfully implemented in many hangover studies (Verster et al., 2019). The hangover condition took place on a morning following an evening of heavy alcohol consumption, and the no-hangover condition on a morning following no alcohol consumption for at least 24 hours prior to testing. Order of testing was counterbalanced across subjects whereby 53% of participants completed the hangover condition first.

7.3.3 Measures

Participants completed three cognitive tasks assessing different components of executive function; switching, updating, and goal maintenance.

7.3.4 Number-Switching Task

A cued-switching task was used to measure switching (Monsell et al., 2003). In this task participants were presented with a string of numbers (1, 2, 3, 4, 6, 7, 8, 9) appearing within a shape (square or diamond). A cue (square/diamond without number) appeared for 650ms before the number stimulus. Participants were instructed to respond depending on the 'rule', which was indicated by the colour of the shape. Participants responded with 'z' if the number was odd or 'x' if the number was even, when presented within a blue shape, and responded with 'n' if the number was lower than 5 or 'm' if the number was higher than 5, when presented within an orange shape. The rule was switched every 4 trials in a sequential manner. The primary outcome measures were switch costs, which were calculated by subtracting RT for the second trial following a rule change (P2) from the first trial following a rule change (P1) and perseveration errors,

i.e., erroneous responses made according to the prior rule set. Schematic representations of each task are presented in Figure 1.

7.3.5 The n-back Task

The letter version of the n-back task was used to measure updating (Attridge et al., 2017). In this task, participants viewed a string of letters (random presentation) and were asked to indicate whether the letter was the same as the letter presented in a previous trial (i.e., n-back). Letters were presented for 500ms with an inter-trial interval (blank screen) for 1500ms. Participants were asked to respond with 'm' when the letter was the same as n-back (target-trials), and 'z' when it was not the same (non-target trials). The task consisted of two 1-back (letter same as the previous trial) and two 2-back (letter same as the one presented before the last trial) blocks presented in alternating blocks (i.e., 1-back, 2-back, 1-back, 2-back). There were 45 trials in each block, with target stimuli (those that are valid n-back trials) presented 33% of the time. The primary outcome measure for this task was errors to target stimuli.

7.3.6 The AX-Continuous Performance Task

The AX Continuous Performance Task (AX-CPT) can be used to assess goal maintenance and can differentiate between proactive and reactive aspects of cognitive control (Braver, Rush, Satpute, Racine, & Barch, 2005; Gonthier et al., 2016; Paxton, Barch, Racine, & Braver, 2008). Participants respond to a probe on the basis of a preceding cue. A letter cue was presented on screen for 500ms followed by a long delay of 4000ms (displayed as '+') (Gonthier et al., 2016). Participants were then presented with a letter probe for 500ms followed by an inter-trial interval of 1000ms (displayed as '****'). Participants responded to probes by pressing 'm' on the keyboard for cue-probe targets or 'z' to non-targets. Target responses are when an 'A' cue is followed by an 'X' probe (AX-type trial), and non-target trials are responses to all other letter sequences. 'AY-type' trials are when an 'A' cue is followed by any probe other than 'X', 'BX-type' trials are those when any cue other than 'A' are followed by an 'X' probe, and 'BY-type' trials occur when any cue other than 'A' is followed by any probe other than 'X'. Target trials (AX) were presented with 70% frequency, and non-targets

with 30% frequency; non-target trial frequency was equally distributed so that non-cue – probe (e.g., BX-type), cue – non-probe (e.g., AY-type), and non-cue – non-probe (e.g., BY-type) trials each occurred 10% of the time. A total of 120 trials were presented in a single block and the primary outcome measure was number of errors for each trial type. Participants utilizing reactive control selectively retrieve contextual information when stimuli are presented, and are less likely to actively maintain contextual information. In the AX-CPT task, reactive control can be observed with increased errors in 'BX-type' trials as participants react to a valid stimulus (the 'X'), but without actively maintaining the preceding invalid cue (not an 'A'). Thus, if individuals with a hangover are biased towards reactive control processes, we would expect to observe an increase in erroneous responses to 'BX-type' trials relative to the no-hangover control condition.

7.3.7 Subjective Measures

Self-reported alcohol consumption on the previous night was used to estimate peak estimated BAC (eBAC) using the Widmark formula (Kypri et al., 2005). Hangover severity was measured using a 1-item hangover severity scale and modified hangover severity scale (mAHSS; (Hogewoning et al., 2016)). Participants were also asked to rate how confident they felt about completing tasks effectively (self-efficacy) on an 11-point scale (0 = *cannot do at all*, 10 = *certainly can do*; Chow et al., 2015) following practice trials on each cognitive task. Following each task, participants were asked to complete a rating scale of mental effort for performance on the respective task (RSME; Zijlstra & Van Doorn, 1985).

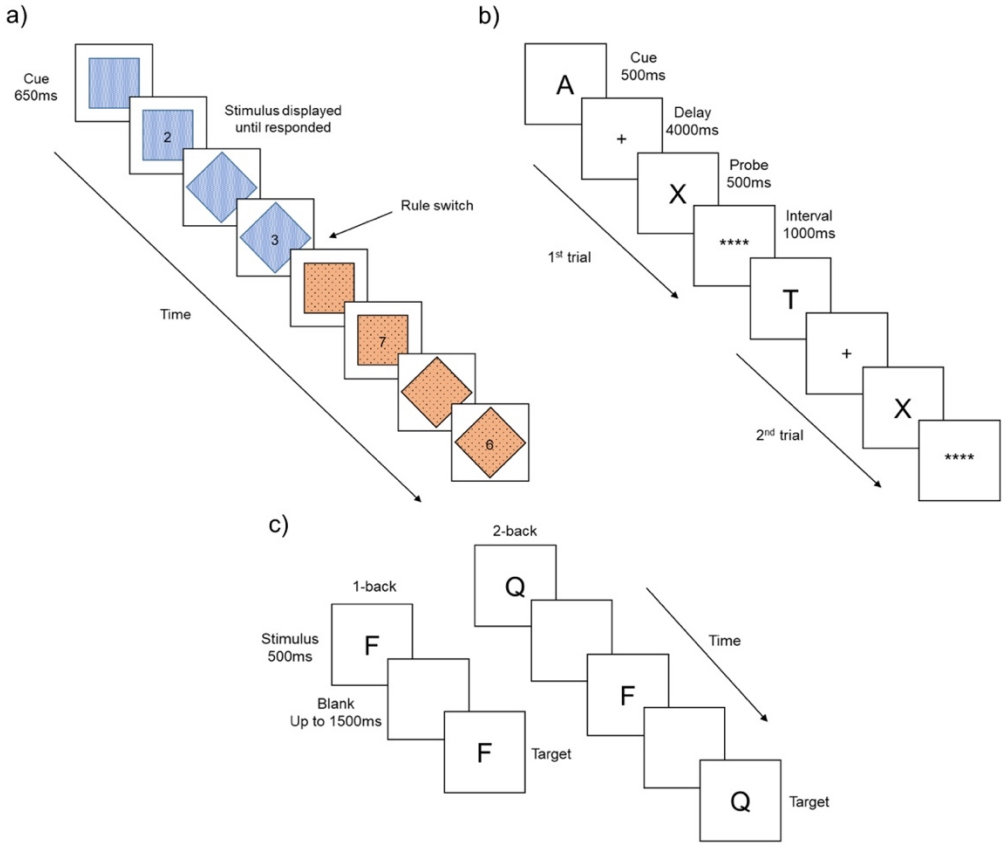


Figure 7.1. Schematic representations of each cognitive task. a) In the switching task participants are presented with a cue (empty blue/orange shape) followed by a number stimulus. Participants respond according to the rule (determine odd/even or higher/lower than 5), indicated by the colour of the shape (blue or orange) b) In the AX-CPT task, participants are presented with a cue-probe pair separated by a long delay. Participants respond by pressing the 'm' key when the cue is 'A' and probe is 'X', otherwise participants respond with the 'z' key. The first trial is an example of a target trial (AX) and the 2nd trial is an example of a BX non-target trial type (the cue is incorrect in this case). c) In the n-back task, participants respond with the 'm' key when the target is the same as the stimulus presented either 1 or 2 trials earlier (e.g., if the target is the same as the previous letter in the 1-back version), otherwise participants respond with the 'z' key.

7.3.8 Procedure

Participants were given information about the study and were booked in for two sessions (hangover, no-hangover) according to when they next expected to experience a hangover or have a no-hangover day. Time of day of testing was similar for both sessions. Participants were screened to ensure they met inclusion criteria and gave written informed consent before the study started. Participants self-reported their previous night alcohol consumption using pictorial prompts labelled with alcohol unit content, and caffeine consumption on

the day of testing. Participants were breathalysed and completed the 1-item hangover severity scale and mAHSS to verify condition (hangover, no-hangover) before completing the three cognitive tasks in a randomised counter-balanced order. Following practice trials participants rated their self-efficacy before completing each task. Following completion of each task, participants completed the RSME. Participants then arranged the second testing session at least 36 hours later to prevent crossover effects. Upon completion of both conditions, participants were paid £10 and received a full debrief.

7.3.9 Statistical Analysis

Statistical analysis was conducted in accordance to our pre-registered protocol (Gunn, Fairchild, Verster, & Adams, 2019). Outliers were removed if they were > 1.5**Inter-Quartile Range* and > 2 *SD* from the mean. For the switching task, trials following an error and trials with RT > 2500 ms were omitted from analysis. Participants for whom < 50% trials were available were removed from analysis (*n* = 5). Error trials were omitted from RT analysis (Longman, Lavric, & Monsell, 2016). Repeated measures ANOVAs were conducted with order and sex as between-subject factors using SPSS (version 25). Effect sizes are reported as Cohen's *d*. Due to the possible effects of acute intoxication at BAC > 0.02% (Holloway, 1994), a sensitivity analysis was conducted to see if residual alcohol concentrations during hangover influenced cognitive performance. A sensitivity analysis excluding one participant with a BAC > 0.02% yielded similar results, therefore this participant is included in the analyses presented below.

7.4 Results

7.4.1 Participant Characteristics

The average age of participants was 20.23 years (*SD* = 2.81; range = 18 - 30) and they consumed an average of 13.28 alcohol units in a typical drinking session (*SD* = 5.13; range = 5 – 28.45). The mean eBAC calculated for the evening before the hangover condition was 0.16% (*SD* = 0.08; range = 0.01% – 0.37%). Although eBAC calculations for some participants were low (e.g., 0.01%), all participants in the hangover condition reported having a hangover (1-item score > 0) and were therefore included in the analysis. A visual

representation of the range of eBAC values in the sample is provided in Figure 2. There was no difference in caffeine consumption between the hangover and no-hangover conditions (p = .781).

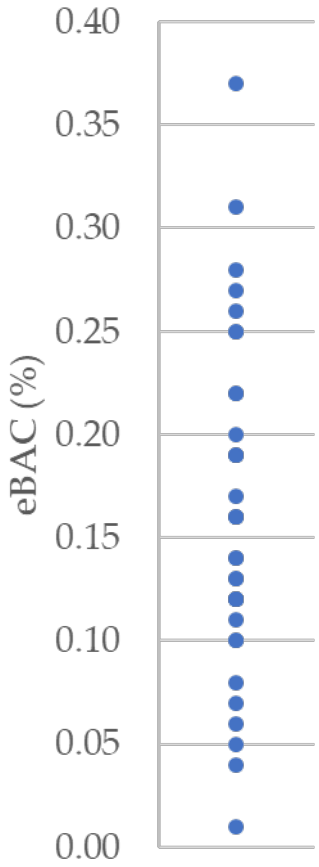


Figure 2. A visual representation of the range of eBAC values during the drinking episode preceding the hangover condition. Each dot represents an individual participant's score.

7.4.2 Effects of Hangover on Switching

For reaction times, analysis of switch costs indicated a trend-level main effect for condition ($F(1, 26) = 3.359$, $p = .078$, $d = 0.72$) whereby switch costs were marginally greater in the hangover relative to the no-hangover condition. There was also a condition*order interaction ($F(1, 26) = 9.850$, $p = .004$, $d = 1.23$) indicating performance improved (lower switch costs) across testing days when the first testing session was the hangover condition ($F(1, 26) = 13.748$, $p = .001$, $d = 1.45$). However, there were no significant differences between testing days for those who completed the task for the second time when hungover ($p = .387$). There were no other significant effects or interactions. Results for main

effects on each task are presented graphically in Figure 3, condition*order interactions are presented in Figure 4, and Means and SDs are presented in Table 1.

For errors, analysis indicated a main effect of condition (F(1, 22) = 6.392, p = .019, d = 1.08) whereby errors were greater overall in the hangover relative to no-hangover condition. There was also a main effect of error-type (F(1, 26) = 77.544, p < .001, d = 3.75) whereby there was a greater number of non-perseveration than perseveration errors. An order*error-type interaction indicated non-perseveration errors were greater for those who completed the no-hangover condition first than those who completed the hangover condition first (F(1, 22) = 8.301, p = .009, d = 1.23) and were greater than perseveration errors in both orders of condition (ps < .001). A condition*order interaction (F(1, 26) = 7.483, p = .012, d = 1.17) indicated that performance significantly declined across testing days when the first testing session was the no-hangover condition (F(1, 22) = 11.650, p = .002, d = .1.45), whereas there were no significant differences between testing days for those who completed the task for the second time when sober (p = .872). Analysis also indicated that participants who were hungover during their second session made greater errors in the hangover condition than those who were hungover during their first session (F(1, 22) = 12.958, p = .002, d = .1.54). A condition*order*error-type interaction indicated that order effects were restricted to non-perseveration errors (F(1, 26) = 6.428, p = .019, d = 1.08), Figure 4b). There were no other significant effects or interactions.

7.4.3 Effects of Hangover on Updating

To investigate the effect of hangover on updating, analysis of each version of the n-back task were conducted separately. For the 1-back version, there was a main effect of condition (F(1, 31) = 20.734, p < .001, d = 1.64), whereby errors were greater in the hangover than the no-hangover condition. There was also a main effect of Trial-Type (F(1, 31) = 25.399, p < .001, d = 1.81), whereby there were a greater number of errors for Target than Non-Target trials. Furthermore, there was a Condition*Trial-Type interaction (F(1, 31) = 7.444, p = .01, d =

0.98). Pairwise comparisons indicated errors were greater in the hangover condition than the no-hangover condition for both Target ($F(1, 33) = 21.700$, $p < .001$, $d = 1.62$) and Non-Target trials ($F(1, 33) = 4.454$, $p = .042$, $d = 0.74$). Furthermore, errors for Target trials were greater than errors for Non-Target trials within both the hangover ($F(1, 33) = 24.087$, $p < .001$, $d = 1.71$) and no-hangover conditions ($F(1, 33) = 19.080$, $p < .001$, $d = 1.52$). There were no other significant effects or interactions.

For the 2-back version of the task, there was a main effect of condition ($F(1, 31) = 20.708$, $p < .001$, $d = 1.63$), whereby errors were greater in the hangover than the no-hangover condition. There was also a condition*order interaction ($F(1, 31) = 6.732$, $p = .014$, $d = 0.93$) that indicated performance significantly improved across testing days for those completing the hangover condition first ($F(1, 31) = 28.528$, $p < .001$, $d = 1.92$), whereas there were no significant differences between testing days for those who completed the task for a second time whilst hungover ($p = .198$; see Figure 4c). Analysis also indicated that participants who were sober during their first session made greater errors in the no-hangover condition than those who were sober during their first session ($F(1, 22) = 12.958$, $p = .002$, $d = .1.54$). There were no other significant effects or interactions.

7.4.4 Effects of Hangover on Goal-Maintenance

Target and non-target trials were analysed separately to avoid comparing stimuli presented 70% of the time to non-target stimuli, which were presented 10% of the time each (Paxton et al., 2008). A 2 (condition) x 2 (order) x 2 (sex) repeated measures ANOVA indicated a main effect of condition only ($F(1, 29) = 16.643$, $p < .001$, $d = 1.52$) whereby AX-type trial errors were greater in the hangover than the no-hangover condition.

Errors for non-target trials (BX, BY, and AY-type trials) were analysed separately. Increased errors on BX-type trials in the hangover relative to the no-hangover condition are indicative of a shift toward a reactive control style. There was a trend-level main effect of condition ($F(1, 28) = 3.279$, $p = .081$, $d = 0.69$)

whereby non-target errors were greater in the hangover relative to no-hangover condition. In addition, there was a main effect of Trial-Type ($F(1, 31) = 28.829$, $p < .001$, $d = 2.84$) whereby there were more errors on AY-type relative to BY-type and BX-type trials and more errors on BX-type relative to BY-type trials. There were no other significant effects or interactions.

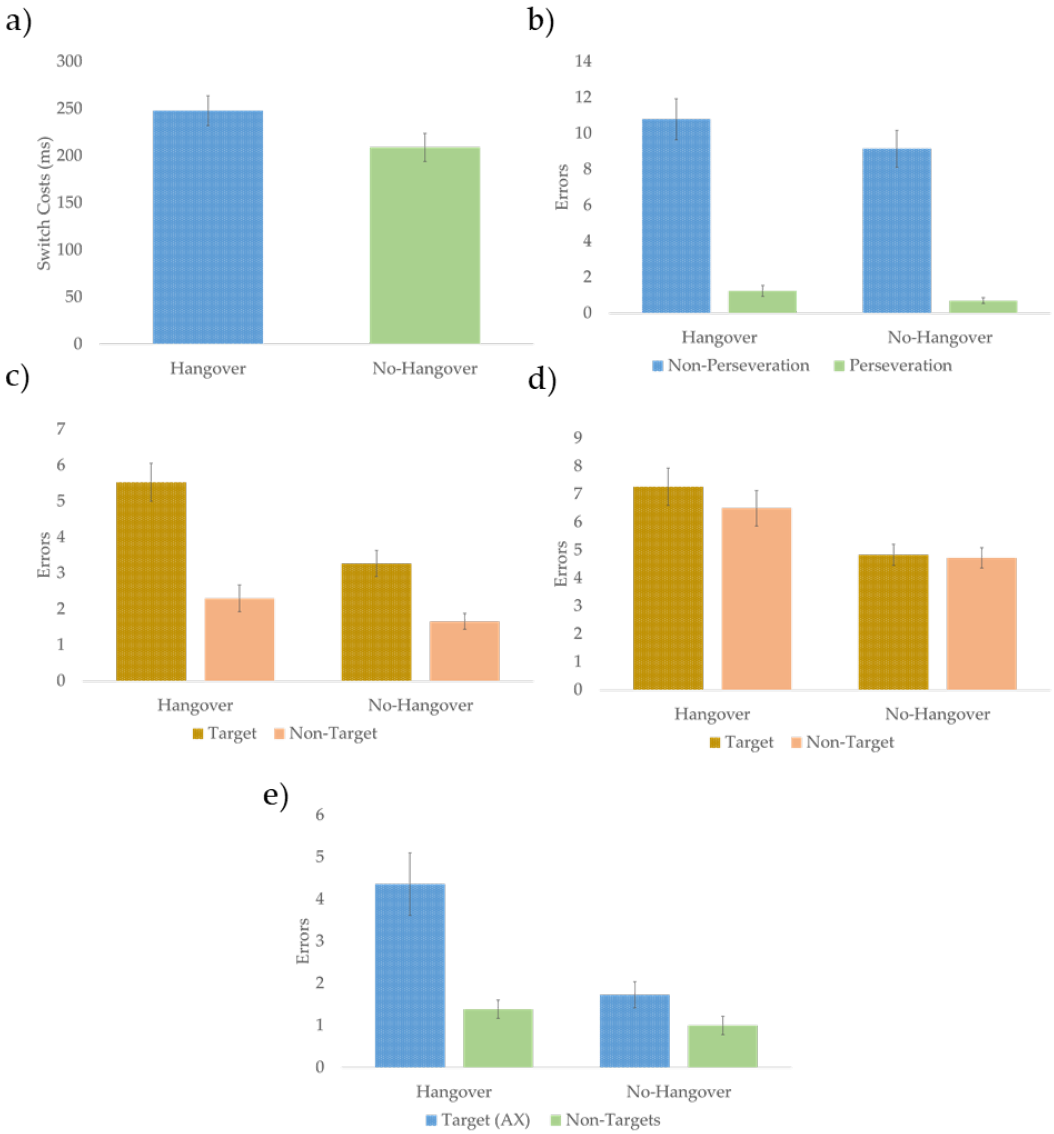


Figure 3. Graphical representations of the main effects from the three cognitive tasks. a) Relative to the no-hangover condition, mean switch costs on the switching task trended toward being greater when individuals were experiencing a hangover. b) Relative to the no-hangover condition, mean errors on the switching task were higher when individuals were experiencing a hangover. c) Relative to the no-hangover condition, errors for non-target and target stimuli in the 1-back version of the n-back task were greater in the hangover condition. d) Relative to the no-hangover condition, errors in the 2-back task were greater overall in the hangover condition. e) Relative to the no-hangover condition, errors on AX trials of the AX-CPT task were greater in the hangover condition. The error bars represent ±1 standard error of the mean.

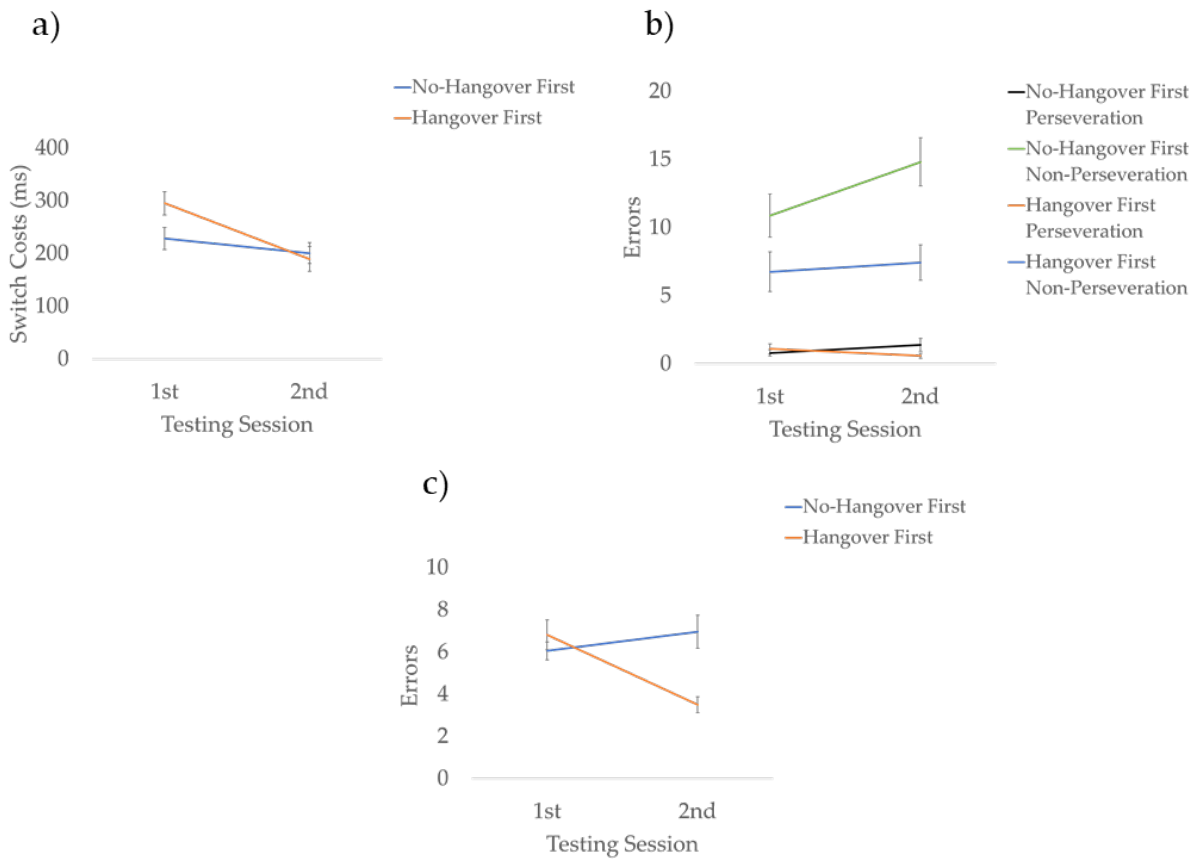


Figure 4. Graphical representations of the condition*order interactions. a) Switching speed decreased (lower switch costs) across testing days when the first testing session was the hangover condition, but not when the first testing session was the no-hangover condition. b) Switching accuracy declined (greater number of non-perseveration errors) across testing days when the first testing session was the no-hangover condition, but not when the first testing session was the hangover condition. c) Updating performance improved (fewer errors) across the testing days for those completing the hangover condition first, but not for those completing the no-hangover condition first. The error bars represent ±1 standard error of the mean.

3.5 Subjective Measures

A series of paired-samples t-tests was used to analyse RSME scores for each task. For the switching task, perceived mental effort was greater ($t(28) = 3.899$, $p = .001$, $d = 0.72$) in the hangover condition than the no-hangover condition. For the n-back task, perceived mental effort was also greater ($t(33) = 3.767$, $p = .001$, $d = 0.65$) in the hangover condition than the no-hangover condition. Furthermore, perceived mental effort for the AX-CPT task was greater ($t(31) =$

2.818, p = .008, d = 0.5) in the hangover condition than the no-hangover condition. There were lower self-efficacy scores in the hangover relative to the no-hangover condition for the switching task ($t(33)$ = 5.816, p < .001, d = 1.00), which trended on significance for the AX-CPT task (p = .051), but not the n-back task (p = .384). There were no gender differences in hangover severity (p = .790) or eBAC (p = .195).

Table 1. *Means, standard deviations, and group comparisons for each variable*

Variable	Hangover		No-Hangover		*p*	*Effect size*
	M	SD	M	SD		
Switching Task						
Switch Cost (ms)	247.83	87.09	208.95	82.27	.078	*d* = 0.72
Switch Errors	6.01	2.97	4.92	2.68	.019*	*d* = 1.08
n-back Working Memory Task						
1-back errors	3.92	1.78	2.47	1.31	< .001*	*d* = 1.64
2-back errors	6.89	3.12	4.78	1.66	< .001*	*d* = 1.63
AX-CPT Task						
Target Errors (AX-type trials)	4.48	4.33	1.79	163	< .001*	*d* = 1.52
Non-Target Errors	1.39	1.24	1.00	1.23	.081	*d* = 0.69
Hangover Severity						
1-Item Hangover Severity	3.83	1.84	0	0	< .001*	*d* = 2.08
mAHSS	2.40	1.31	0.24	0.26	< .001*	*d* = 1.72
Subjective Measures						
RSME Switching	77.27	23.7	58.72	22.78	.001*	*d* = 0.72
RSME n-back	76.41	24.22	58.79	20.81	.001*	*d* = 0.65
RSME AX-CPT	59.69	23.70	47.41	28.67	.008*	*d* = 0.55
Self-efficacy Switching	6.88	2.14	8.76	1.28	< .001*	*d* = 1.00
Self-efficacy n-back	6.31	2.18	6.74	2.5	.384	*d* = 0.14
Self-efficacy AX-CPT	8.53	1.38	9.06	1.41	.051	*d* = 0.35

Note: M, mean; SD, standard deviation; mAHSS, modified Alcohol Hangover Severity Scale; RSME, Rating Scale of Mental Effort. The asterisk indicates that the difference between the hangover and no-hangover conditions was significant.

7.4.6 Correlational Analysis

Bivariate correlational analysis provided no evidence that either hangover severity scores (as measured by the mAHSS; *ps* > .178) or self-efficacy scores (*p*s > .098) were associated with performance on the switching, n-back or AX-CPT tasks. Bivariate correlational analysis also provided no evidence that eBAC was related to hangover severity (p = .229) or task performance (*p*s ≥ .161).

7.5 Discussion

This study demonstrated that switching, updating, and goal maintenance are all impaired during alcohol hangover. Thus, in terms of the unity/diversity model of

executive functions (Friedman & Miyake, 2017), all of the core components of executive function appear to be negatively influenced by hangover. Errors for non-target trial types on the AX-CPT task (i.e., AX-type, BX-type, or BY-type trials) showed a trend towards being greater in the hangover than the no-hangover condition; however, contrary to our hypothesis, BX-type errors did not differ between conditions. Also contrary to our hypothesis, there was no evidence that performance on switching, updating, and goal-maintenance tasks was related to hangover severity. There was also no evidence that hangover-related impairments were related to self-efficacy during switching, updating, and goal-maintenance task performance. However, the participants felt that they needed to expend greater mental effort to complete each task when experiencing a hangover than when not hungover. Furthermore, there was no influence of sex on cognitive performance when hungover for any of the tasks.

In-line with a previous naturalistic study of hangover (Devenney & Verster, 2019), our results from the switching task indicate that individuals make a greater number of errors, reflective of deficits in task switching, when they are experiencing a hangover than when not hungover. This suggests that hangover impairs an individual's ability to switch attention from one task or mental set to another effectively. Although studies that experimentally induce hangover often administer lower doses of alcohol than observed in real-life drinking (Gunn et al., 2018), our null results for an effect of hangover on switch costs are in-line with previous experimental research (Wolff et al., 2016). Therefore, it appears as though individuals may maintain speed of switching, but become less accurate when experiencing a hangover compared to no-hangover. For switching, our results also tentatively indicated an interaction of condition with order which further suggests a speed-accuracy trade off. Those completing the hangover condition first appear to sacrifice time (switch costs) to maintain accuracy during the hangover condition, whereas those completing the hangover condition second appear to sacrifice accuracy to maintain speed.

Our results indicate poorer performance on both the 1-back and 2-back versions of the n-back task in the hangover compared to no-hangover condition.

This suggests that an individual's ability to update information in working memory is impaired during hangover. As the 1-back version of the task is relatively easy and places a comparatively low load on working memory, the current results suggest that participants with a hangover experienced an increased cognitive load, relative to during a non-hungover state. This is in line with previous research suggesting that hangover reduces the amount of cognitive resource available (Scholey, Ayre, et al., 2019; Wolff et al., 2016), and is consistent with our results indicating greater mental effort to complete tasks. Although hangover symptoms such as headache and fatigue are known to impair an individual's ability to update information via increased cognitive load (Moore et al., 2013), our results indicate no evidence of an association between performance on any task and overall hangover severity scores. This suggests that hangover-related impairments in executive functions are likely due to factors other than simple cognitive interference due to the presence of negative symptoms. For example, it is possible that physical alterations in hangover, such as dopaminergic or noradrenergic transmission (Howse et al., 2018; Maki et al., 1998), or immune effects (indexed via cytokine levels) (Kim et al., 2003; A Van de Loo et al., 2015), influence cognition (Tipple et al., 2017). The observed interaction of condition and order tentatively suggests that those completing the hangover condition first appear to have a greater improvement in their second session than those completing the no-hangover condition first. This could indicate an expectancy effect whereby, when the first condition is during a hangover, participants expect their second performance on the task (i.e., when sober) to be greatly improved.

Results from the current study indicate poorer goal-maintenance during hangover, as reflected by a greater number of errors on the core AX trials of the AX-CPT task in the hangover compared to no-hangover condition. This suggests that an individual's ability to maintain and manage goals is impaired whilst experiencing a hangover. Goal maintenance is thought to represent the 'common factor' of the unity/diversity model and an important aspect of maintaining goals is inhibitory control (Friedman & Miyake, 2017). Therefore, impaired goal maintenance in hangover may contribute toward findings of previous studies of executive functions, which have indicated impaired

prospective memory, semantic verbal fluency (Heffernan et al., 2019), working memory, (Howland et al., 2010), and inhibitory control (Devenney & Verster, 2019; Gunn, Verster, et al., 2019; McKinney, Coyle, Penning, et al., 2012) during a hangover relative to a no-hangover condition. Contrary to our hypothesis, there was no evidence that participants were biased toward reactive control during a hangover, suggesting participants engage in proactive control during this task, but are ineffective in doing so (as evidenced by increased errors on the core AX-type trials). However, it is possible that the current study did not have sufficient power to observe effects on reactive control due to the low number of non-target trials on this task. As goal maintenance is important for many everyday behaviours that rely on executive functions, such as planning, decision making, organising, and other 'higher-order' skills, future studies should investigate the influence of hangover on these processes.

The current results should be viewed in light of the following strengths and limitations. The crossover, within-subjects design could be considered a strength of the current study because each subject serves as their own control. Furthermore, the naturalistic design, which is favoured by many researchers in the field, could be considered a strength as it involves investigating the impact of real-life drinking, rather than experimentally induced hangover which might involve consuming lower levels of alcohol (Verster et al., 2019). However, the study is limited in its ability to generalise beyond the narrow demographics of this student population (i.e., to other age groups, education levels etc.). Another limitation is the use of the Widmark formula, which should be viewed as a rough estimate of alcohol consumption. Future studies should explore directly measuring BAC during the heavy drinking occasion, possibly via wearable technology. Although each task used in this study was chosen to reflect switching, updating, or goal maintenance, these tasks are cognitively complex (i.e., they measure multiple executive and non-executive functions). One technique that could be utilised in future studies to overcome variability attributable to task stimuli, rather than the respective executive function component, is the adoption of a latent variable approach, which is a statistical technique that can capture common variance across multiple measures (e.g., Korucuoglu et al., 2017).

7.6 Conclusions

Results from the current study indicate that all domains of the unity/diversity model of executive functions are negatively affected by alcohol hangover. Executive functions are important cognitive processes which are utilised in everyday behaviours, such as planning, decision-making, and emotion regulation. Thus, impairments in executive functions could have broad implications for a wide variety of everyday activities, including in the workplace. For example, employees who go to work when experiencing a hangover may negatively influence the productivity and working environment of others (Bhattacharya, 2019). Future studies should aim to investigate the impact of hangover-induced executive dysfunction on the performance of everyday tasks.

7.7 Additional Analysis

As with previous experimental work in this thesis, the relationship between hangover severity (as measured by mAHSS) and alcohol consumption (eBAC), and gender differences were explored. Bivariate correlational analysis indicated no association between hangover severity and alcohol consumption (r = .154, p = .37, 95%CI [-0.15 – 0.50]). Independent t-tests indicated no gender differences for hangover severity (p = .937), but there was a trend level significance for gender differences in alcohol consumption (p = .078), whereby female participants had a greater eBAC than male participants.

Results from this additional analysis indicate no association between hangover severity and alcohol consumption. This is in-line with the experimental work presented in Chapter Five, but in contrast to the experimental work presented in Chapter Six and previous studies (Scholey, Benson, et al., 2019b; Stephens et al., 2017). The reason for these mixed findings is unclear. However, given the methodological similarity in the three studies presented in this thesis it is possible to combine data across studies to develop a larger sample. Results from the combined data set and discussion of findings are presented below. Our analysis (section 7.4) also indicated no gender differences for the effects of hangover on all executive function tasks. Previous studies have produced mixed results for gender effects of hangover on memory, with some reporting

impairments in short-term memory for females only (Howland et al., 2010), whereas others report no gender differences (Verster et al., 2003). Throughout the experimental work in this thesis no gender differences have been found for the cognitive effects of hangover.

7.8 Combined Analysis

7.8.1 Introduction

In the 'Additional Analysis' sections of each experimental study (Chapters Five, Six, and Seven) there have been mixed findings for the relationship between hangover severity and alcohol consumption. Given the mechanistic link between alcohol consumption and alcohol hangover, the results of Chapters Five and Seven, which reported no correlation between hangover severity and alcohol consumption, were surprising. In contrast, Chapter Six found hangover severity and alcohol consumption were positively correlated. Furthermore, recent survey data has indicated that women consume fewer alcoholic drinks than men on occasions resulting in a hangover, but there are no gender differences in overall hangover severity (van Lawick van Pabst, Devenney, & Verster, 2019). However, each of the experimental studies presented in this thesis found no difference between male and female participants for overall hangover severity or alcohol consumption (see Additional Analysis sections in Chapters Five, Six, and Seven). As each study presented in this thesis utilised a naturalistic design and used the same measures for alcohol consumption and hangover severity, data were combined to obtain a larger and more representative sample. These combined data were then used to provide additional clarity to mixed findings regarding the relationship between hangover severity and alcohol consumption and to further explore gender differences in hangover severity and alcohol consumption.

7.8.3 Gender differences in hangover severity and alcohol consumption

The combined data set consisted of 117 participants in total (57 male, 60 female). An independent t-test indicated that there was no difference in hangover severity (as measured by mAHSS) between male and female participants ($t(115) = 0.422$, $p = .674$, $d = 0.04$). A further independent t-test

also indicated no difference in alcohol consumption (as measured by eBAC) between male and female participants ($t(114) = 0.886$, $p = .377$, $d = 0.08$). However, male participants did consume more units of alcohol the night before experiencing a hangover than female participants ($t(115) = 3.940$, $p = .001$, $d = 0.36$) – which is consistent with the literature (Wilsnack et al., 2000). As eBAC calculations take into consideration body weight (which is typically higher in males) and gender differences in alcohol metabolism, higher unit consumption in males is logically consistent with the finding of similar eBAC levels between male and female participants. Table 7.2 shows mean scores and SD of hangover severity and alcohol consumption for male and female participants.

Table 7.2. Alcohol Consumption and Hangover Severity for the Combined Data Set

	All, *n* = 117		Male, *n* = 57		Female, *n* = 60	
	Mean	SD	Mean	SD	Mean	SD
mAHSS	2.79	1.56	2.85	1.44	2.73	1.69
eBAC	0.17%	0.08	0.16%	0.07	0.18%	0.09
Units	14.27	5.77	16.30	6.35	12.34	4.40

7.8.4 Alcohol consumption and Hangover Severity

Bivariate correlational analysis indicated that alcohol consumption (as measured by eBAC) is positively associated with hangover severity (as measured by mAHSS), $r = .254$, $p = .006$, 95%CI [0.06 – 0.42], Figure 7.3.

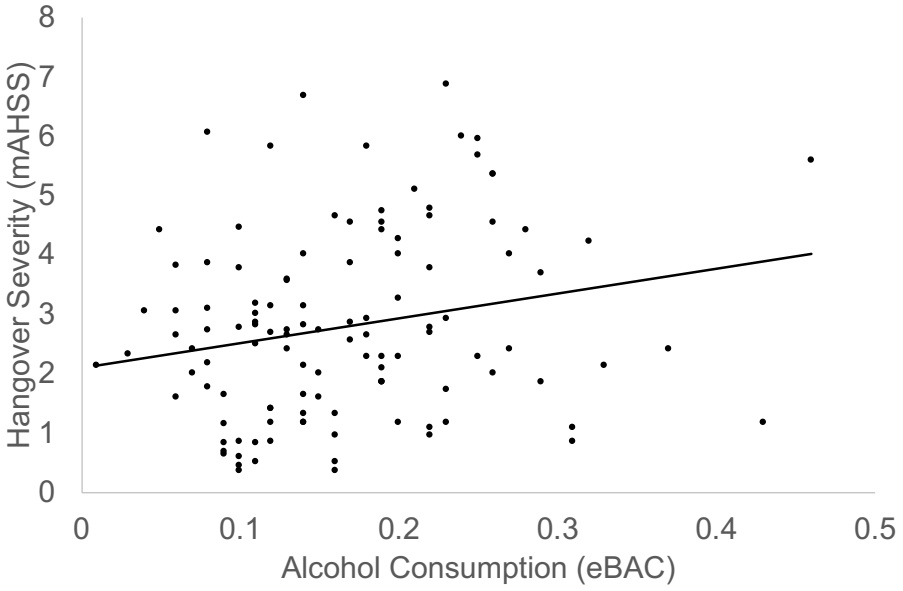


Figure 7.3. Scatter plot of scores from the combined data set highlighting a positive association between hangover severity (y-axis) and alcohol consumption scores (x-axis), $r = .243$, $p = .006$.

In summary, the combined data analysis presented in this section indicates that alcohol consumption positively correlates with hangover severity, suggesting that as alcohol consumption increases, hangover severity also increases. Furthermore, analysis of the combined data set indicates that neither alcohol consumption nor hangover severity differed between male and female participants. The following Chapter will present a detailed discussion of the main findings of this thesis, as well as the additional and combined analysis.

Chapter Eight: General Discussion

8.1 Overview

This chapter summarises findings of the studies presented in this thesis and explores the implications for the influence of alcohol hangover on cognition and the role of hangover in future alcohol consumption. It also discusses the secondary findings of experimental studies and findings from combined data across all experimental studies to obtain a larger and more representative sample. Furthermore, this chapter will discuss the broader implications of the findings presented in this thesis, such as possible influence of hangover on workplace productivity and driving. Alongside findings of studies in this thesis, limitations of the research and suggestions for future research are discussed.

8.2 Main Findings

8.2.1 A Systematic Review of the Next-Day Effects of Heavy Alcohol Consumption on Cognitive Performance

Overall, this thesis aimed to better understand the cognitive effects of alcohol hangover. To achieve this, studies were designed to address four aims. Given mixed findings and the paucity of hangover research in the literature, the first aim of this thesis was to synthesise findings and provide clarity by conducting a systematic review and meta-analysis (Chapter Three). Results indicated that hangover impairs core cognitive processes. Specifically, the meta-analysis indicated that short- and long-term memory, sustained attention, and psychomotor skills were all impaired by hangover. The review also highlighted that driving, which utilises sustained attention and psychomotor skills (Allen et al., 2009), is impaired during hangover compared to a no-hangover control. This suggests that alcohol hangover negatively influences cognitive functions that are important for everyday task performance. However, it was evident from the review that few studies had explored the effects of alcohol hangover on higher-order cognitive processes – which were addressed in the experimental work described in this thesis. A further key findings was issues about the quality of research in this field, highlighting the need to develop and utilise rigorous methodology that reflect real-life alcohol hangover.

8.2.2 The Effects of Alcohol Hangover on Response Inhibition and Attentional Bias Toward Alcohol-Related Stimuli

Hangover has previously been linked to the development of alcohol use disorder; however, the mechanisms contributing toward this link were unclear. As models of alcohol addiction theorise that enhanced salience of alcohol-related cues, poor executive functions, and greater negative affect contribute to alcohol use disorder (Koob, 2013), the second aim of this thesis was to investigate the effect of alcohol hangover on these processes. Chapter Four presents work that contributed toward the development of stimuli for an alcohol-related attentional-bias task utilised in the experimental work presented in Chapter Five. Results indicated that response inhibition was impaired and mood lower in the hangover relative to no-hangover control condition. However, there was no evidence to support our hypothesis of an attentional avoidance of alcohol-related stimuli during hangover, nor was their evidence of a bias towards alcohol-related stimuli. There was also no evidence of an attentional bias toward alcohol-related stimuli in the no-hangover condition, possibly indicating that the stimuli in the Visual Dot Probe task, or the task itself was not reliable to observe effects.

8.2.3 Does Alcohol Hangover Affect Emotion Regulation Capacity? Evidence from a Naturalistic Cross-Over Study Design

In addition to influencing cognition, hangover also leads to negative affect in many individuals (McKinney, 2010). Negative affect can contribute toward the development of future alcohol-related problems as individuals may choose to drink to reduce negative feelings (Koob, 2013), and could contribute toward poor productivity when working with a hangover (Bhattacharya, 2019). The third aim of this thesis was therefore to investigate the effect of hangover on emotion regulation – a key process in modulating emotional expression and experience (Gross, 1998b). Results from a lab-based task indicated no difference between conditions on emotion regulation. However, stimuli were rated as lower in affective valence during the hangover condition, implying a general negative shift. Results from a questionnaire measure of emotion regulation in everyday life indicated poorer emotion regulation in hangover relative to a no-hangover

control condition. Furthermore, participants indicated poorer responses to and perception of emotional states, greater difficulties with modulating emotional and behavioural responses, and greater problems in identifying emotional states during a hangover. However, participants had similar awareness of emotions between conditions.

8.2.4 The Effects of Alcohol Hangover on Executive Functions

The fourth and final aim of this thesis was to investigate the effect of hangover on core components of executive functions. As suggested by the unity/diversity model of executive functions, these core components are switching, updating, and goal-maintenance (Friedman & Miyake, 2017). Previous research has found that hangover can impair working memory (Howland et al., 2010), prospective memory and semantic verbal fluency (Heffernan et al., 2019), and interference control (Devenney & Verster, 2019; McKinney, Coyle, Penning, et al., 2012). However, few studies had been informed by contemporary models of executive functions to test all three core components at once; i.e., the ability to switch attention, update information, and maintain goals in working memory. Results indicated poorer switching, impaired updating, and impaired goal-maintenance during a hangover compared to the no-hangover condition. Together these results suggest that all three components of executive functions proposed by the unity/diversity model are impaired in hangover.

8.3 Discussion of Key Findings

8.3.1 The Cognitive Effects of Hangover

The novel findings of our systematic review provide some clarity to the previously mixed literature and suggest that core cognitive functions are impaired in hangover. When the data were combined in a meta-analysis, overall effect estimates indicated that both short- and long-term memory were impaired during hangover. Furthermore, overall effect estimates of sustained attention and psychomotor speed indicated impairments during hangover, but not divided attention. Two recent studies, that were conducted after the meta-analysis, provide additional support for our results (Devenney et al., 2019; Devenney &

Verster, 2019). These studies both used a naturalistic design and measured short-term memory and psychomotor speed. One recruited from a student population and also measured divided attention (Devenney & Verster, 2019), and the other from a non-student population (Devenney et al., 2019). Results from both studies indicate that participants recall fewer items in tests of short-term memory, and take longer to respond in choice RT tasks when hungover compared to a no-hangover control. In addition, results from a divided attention task indicated no effect of hangover (Devenney & Verster, 2019).

The experimental work in this thesis went on to study areas of cognition that have previously received little attention in hangover research, i.e., executive functions and affective processes related to EFs. The results indicate that hangover impairs higher-order cognitive functions such as response inhibition, switching, updating, and goal maintenance. The study presented in Chapter Five was the first to investigate the effects of hangover on response inhibition and attentional bias towards alcohol-related stimuli using a naturalistic design. Our finding of poorer response inhibition in hangover is in-line with studies that have found impaired interference control (Benson et al., 2018; Devenney & Verster, 2019; McKinney, Coyle, Penning, et al., 2012), but are in contrast to recent experimental studies that found no effect of hangover on response inhibition or interference control (Opitz et al., 2019; Zink et al., 2018). Similarly contrasting results between methodological designs are found when investigating psychomotor skills in hangover (i.e., naturalistic designs observe impairments whereas experimental designs do not). It is therefore likely that aspects of naturalistic hangover, which are not included within experimental designs, contribute toward cognitive impairments. One possibility is the higher levels of alcohol consumption in naturalistic designs. However, it should be noted that no relationship between alcohol consumption and cognition in hangover was found in the current studies (see 'Additional Analysis sections for Chapters Five, Six, and Seven). It may be that the increase of alcohol consumption during heavy drinking relative to normal alcohol consumption is important in predicting hangover severity – and possibly cognitive effects (Verster et al., 2020). Therefore, future research should investigate how each

methodological design differs in terms of the relative increase in alcohol consumption to understand the differential effects of each design.

To our knowledge, the work presented in Chapter Seven is the first to explore the effects of alcohol hangover on core components of executive functions. In terms of the unity/diversity model, executive functions are comprised of the core components: switching, updating, and goal maintenance – all of which were found to be impaired by hangover. As goal maintenance reflects a common factor that is utilised in all tasks of executive functions, our results suggest impairments in core executive functions may contribute to the previously-reported effects of hangover on prospective memory (Heffernan, 2018; Heffernan et al., 2019), working memory (Howland et al., 2010), verbal semantic memory, (Heffernan et al., 2019), and reward learning (Howse et al., 2018). Our results also imply that other behaviours that utilise executive functions (e.g., decision-making, planning, and problem solving) may be influenced by hangover. This is something future research should investigate further. Furthermore, future research could explore the effect of hangover on real-world behaviours and executive functions in the same study to examine the impact of hangover-induced executive function deficits in real-life situations.

Our novel findings of impaired executive functions and other core cognitive functions suggest hangover may contribute to poorer performance of everyday behaviours – for example, our finding of greater perceived difficulties in regulating emotions. Effective emotion regulation requires inhibition of stimuli that may interfere with the desired regulation (e.g., preventing unwanted thoughts (Joormann, 2010)). Effective emotion regulation also requires switching attention form one mental set to another, and to maintain goals (i.e., to regulate the emotion). Chapters Five and Seven indicate that inhibition, switching, and goal maintenance are all impaired in hangover, suggesting that the influence of hangover on these cognitions may contribute to greater perceived emotion dysregulation observed in Chapter Six. However, as regulation was unaffected by hangover in the lab-based emotion regulation task in Chapter Six, it is possible that these adverse effects could be overcome if an

individual increases their effort to engage in cognitive reappraisal strategies. It is therefore important that future studies examine emotion regulation in a more naturalistic or implicit way to see whether findings correspond more closely to the emotion regulation questionnaire when participants are not explicitly exerting additional effort to complete a lab-based task. Together, these results suggest that hangover-related impairments in cognitions may negatively influence important everyday behaviours that utilise executive function processes, such as decision-making or problem solving.

The results presented in this thesis also have implications for the cognitive processes that contribute toward future alcohol consumption. Models of substance use suggest that alcohol use disorder develops when alcohol-related cues become more salient, and when alcohol use leads to impaired executive function and disrupted mood (M. Field et al., 2010; Goldstein & Volkow, 2002; Jentsch & Taylor, 1999; Koob, 2013). Furthermore, emotion dysregulation may contribute to increased relapse vulnerability in alcohol-dependent patients (Fox, Hong, & Sinha, 2008). Although our results suggest being hungover does not influence attentional bias towards (or away from) alcohol-related cues (Chapter Five), there are deficits in executive functions (Chapter Five and Seven), lower mood, and greater emotion dysregulation (Chapter Six) during hangover relative to when not hungover. Therefore, hangover produces deficits in cognitive processes that are thought to contribute toward future alcohol use. These results may underlie findings of previous hangover research that has linked hangover frequency to alcohol use disorder (Courtney et al., 2018; Piasecki et al., 2010), and the link between using alcohol as hangover relief and greater symptoms of alcohol use disorder (Hunt-Carter et al., 2005). However, as the experimental research in this thesis did not directly measure future alcohol consumption, further research is needed to establish how impairments in these cognitive processes contribute to future alcohol use.

8.3.3 The Naturalistic Methodology

Previous reviews examining the cognitive effects of alcohol hangover have presented mixed results, suggesting these may have arisen due to variety in

definitions of a hangover, methodological design, and low methodological rigour (Prat et al., 2008; Stephens et al., 2014, 2008). In Chapter Two the methodology of hangover studies was critically examined, and a methodological design that addresses previous limitations was developed to be used in experimental work throughout the thesis. All experimental work in this thesis utilised a within-subjects 'naturalistic' design, whereby participants completed a hangover condition the morning following a night of planned heavy drinking, and a no-hangover control condition (no alcohol for at least 24 hours prior to testing). The naturalistic design enables hangover researchers to examine the effects of alcohol hangover after a night of alcohol consumption comparable to normal drinking as researchers do not interfere with a participant's drinking behaviour (Verster et al., 2019).

The methodological approach was refined throughout each study of this thesis, mainly in terms of optimising recruitment of participants – which can be particularly challenging in hangover research. Chapter Five outlines an approach designed to control for as many extraneous variables as possible and included three sessions (screening, hangover condition, no-hangover condition). However, recruitment was slow and participant numbers limited. Therefore, Chapter Six allowed a more flexible approach, with two instead of three sessions (a separate screening session was dropped), which utilised participant harvesting recruitment strategies and participants could be tested in the location they were approached. This approach worked well, but participants who were approached tended to book testing sessions, rather than take part then and there. Therefore, Chapter Seven utilised a two-session methodological approach, but maintained a rigorous design – with sessions booked in advanced and testing conducted in a laboratory setting at the University of Bath where extraneous variables (e.g., noise) could be controlled. Attrition rates for each study were 37%, 22%, and 8% respectively, suggesting that the methodological approach of Chapter Seven could become a model for hangover research going forward.

8.4 Discussion of Additional and Combined Findings

Alongside the main aims of this thesis, experimental studies also explored the relationship between hangover severity, alcohol consumption and cognition. Furthermore, each study explored the influence of hangover on perceived mental effort to complete tasks, as well as gender effects. The findings from these analyses and findings from data combined across the three studies are discussed below.

8.4.1 Mental Effort in Hangover

Across all studies presented in this thesis, participants reported greater perceived mental effort to complete cognitive tasks in the hangover relative to no-hangover condition (Chapters Five, Six, and Seven). Mental effort can be influenced by cognitive load and therefore is often considered an indication of available cognitive resource (Sergeant, 2000). Therefore, results from all studies in this thesis suggest that fewer cognitive resources are available during a hangover. This is in-line with other research suggesting hangover reduces cognitive resource (Scholey, Ayre, et al., 2019; Wolff et al., 2016). As mentioned in Chapter One, there are many factors that could increase cognitive load during a hangover, including physiological alterations such as increased cortisol (Linkola et al., 1976). However, the precise mechanisms that underlie increased cognitive load in hangover are yet to be determined and should be a focus of future research.

8.4.2 Hangover Severity and Cognition

For all experimental studies presented in this thesis (Chapters Five, Six, and Seven), there was no association between hangover severity and performance on cognitive tasks. These findings are in contrast to previous research that did link hangover severity to cognitive performance (Rohsenow et al., 2010; Scholey, Benson, et al., 2019a). These findings are somewhat surprising given the wealth of research outside of the hangover literature that suggest individual symptoms (e.g., headache) interfere with cognitive processes (see section 1.2). It is possible that a link between individual symptoms that are known to interfere with cognition was masked by the use of overall hangover severity scores to

measure associations between hangover severity and cognitive performance, rather than individual symptom severity. However, as the experimental studies were not powered to test for associations between individual symptoms and cognitive performance, this analysis would not have been not appropriate.

8.4.3 Alcohol Consumption and Hangover Severity

The 'Additional Analysis' sections in Chapters Five, Six, and Seven highlight that alcohol consumption (as measured by eBAC) correlated with hangover severity (as measured by mAHSS) in Chapter Six, but not Chapters Five and Seven. However, when data from the three experimental studies were combined into a larger sample (see 'Combined Analysis'), results indicated that alcohol consumption is associated with hangover severity. Therefore, hangover severity is related to the estimated peak alcohol concentration achieved during a night of heavy alcohol consumption – a finding that fits a common sense model and adds validity to the self-reported measures of hangover used in this thesis.

8.4.4 Gender Differences

Each experimental study of this thesis also explored gender differences in the cognitive effects of alcohol hangover. Some previous research has suggested that the effects of hangover on short-term memory may be influenced by gender (Howland et al., 2010), whereas others have found no interaction between hangover condition and gender (Verster et al., 2003). Our results, presented in the 'Additional Analysis' section for each study, highlighted that the effects of hangover on executive functions were not influenced by gender. There were also no gender differences for hangover severity or alcohol consumption in each study. Gender differences for hangover severity and alcohol consumption were also explored when data from the three studies were combined. Results from the combined analysis indicated no difference between male and female participants in hangover severity or alcohol consumption. Therefore, in the current sample, our results suggest that neither alcohol consumption, hangover severity, nor cognition during a hangover is influenced by gender. However, it

should be noted that these results need to be replicated in larger, more representative samples.

8.5 Strengths and Limitations

The findings of this thesis should be viewed in light of the following strengths and limitations. A strength of the research conducted in this thesis is the consideration of the tasks utilised to measure each cognitive domain. Each task was carefully chosen based on sensitivity to alcohol or hangover-related effects to best represent the cognitive construct investigated. Furthermore, the methodological approach developed throughout this thesis addresses limitations of previous research to increase rigour and has greatly improved rates of participant retention. As the naturalistic approach reflects real-life drinking and other behaviours such as dancing and changing of venues (Verster et al., 2019), the applied methodology of the current thesis could be used as a model for future hangover research. However, there are still limitations within this approach. For example, accurately measuring peak blood alcohol concentration. eBAC calculations are widely used in naturalistic hangover studies (e.g., Scholey, Benson, et al., 2019a), but should only be considered an indication of peak BAC and not a true reflection of BAC. As practical and ethical considerations restrict researchers' abilities to measure BAC during a participant's heavy drinking occasion, calculating eBAC has been a reasonable approach. However, with the emergence of new technologies, such as wearable devices that measure alcohol concentration, this limitation may be overcome in future research.

As some effects that have been observed in student populations (e.g., switching; Devenney & Verster, 2019) have not been replicated in non-student samples (Devenney et al., 2019), the results from studies in this thesis are limited in their ability to generalise beyond the narrow demographics of participants. Therefore, further studies should assess hangover-related effects on executive functions, emotion regulation, response inhibition, and attentional bias towards alcohol-related stimuli in broader samples (i.e., different age groups, non-student samples, different education levels etc.).

8.6 Implications of Findings

The findings of this thesis have many implications for both future research and in the real-world. As mentioned above, the methodology that was developed throughout the thesis could be used as a model to be used in future research. Further advances in technology (e.g., wearable devices) could add additional control to the naturalistic approach. For the real-world, our findings imply that behaviours which rely on core cognitive functions (e.g., memory) or executive function processes may be negatively influenced by an alcohol hangover. Decision-making, problem solving, and risk-taking are all behaviours that utilise executive functions and are highly important in many workplace settings. For example, whilst working in fast-paced environments such as the NHS, an employee would need to weigh up risk to make decisions about an individual's care and overcome a multitude of problems to deliver quality care. Our findings suggest that performance in positions that rely on these processes may become impaired the morning after a night of heavy drinking, which in-turn could contribute toward the vast economic consequences of hangover (Bhattacharya, 2017, 2019). Furthermore, our findings from the systematic review highlighted impairments in core cognitions which are important for driving (sustained attention and psychomotor skills). As some individuals choose to drive with a hangover (Verster, Van Der Maarel, McKinney, Olivier, & De Haan, 2014), and driving performance can be impaired (Alford et al., 2018; Verster, Bervoets, et al., 2014), these findings have potentially serious implications for driving safety.

8.7 Future Research

Findings of the current thesis leave open several avenues for future research. One is the exploration of underlying factors contributing toward the cognitive impairments observed here. Of particular interest would be how factors in the naturalistic design contribute toward hangover effects. Studies should also investigate the effect of alcohol hangover on everyday behaviours that rely on executive functions and are important for good workplace performance. These could include decision-making, problem-solving, and/or risk-taking. Research should also explore how hangover influences workplace performance in settings where these cognitions are highly important (e.g., in the health and social care

industry) or potentially dangerous (e.g., transport). Furthermore, studies of hangover in 'high-risk' industries, such as healthcare, finance, or the military, could be conducted to develop greater insights into the real-world impact of hangover. This is of particular importance as, as our findings suggest, hangover can impair an individual's thought processes yet there are no regulations regarding attending work the morning after a night of heavy drinking. The methodological design developed in this thesis allows an ideal paradigm in which to investigate these cognitions. Research should also explore how the cognitive deficits observed in the current thesis contribute toward future alcohol use (e.g., does hangover-induced impairments in executive function lead to a greater probability of consuming alcohol within the next few days?). In addition, studies should investigate the influence of hangover on cognition over time (e.g., the length of time hangover-related impairments last) and in a real-life setting. For example, exploring which emotion regulation strategies are typically used during a hangover, how these differ to when not experiencing a hangover, and how effective these strategies are. This could be done by utilising techniques that allow for testing at multiple time points through online apps (i.e., electronic momentary assessment) alongside new technology that measures BAC in real-time (e.g., wearable devices).

8.8 Conclusion

The results from studies presented in this thesis indicate that both core cognitive processes (memory, sustained attention, and psychomotor speed) and 'higher-order' executive functions (updating, switching, goal maintenance, and inhibition) are impaired during alcohol hangover. Furthermore, participants perceived greater difficulty in regulating emotions during a hangover, although emotion-regulation was unaffected by hangover in a lab-based emotion regulation task. Hangover-related impairments in these cognitive processes may contribute toward hangover-related impairments in behaviours that utilise these cognitions, such as driving or decision making. Furthermore, impairments in these cognitive processes could contribute toward poor workplace performance in hangover (e.g., workplace conflicts (Ames et al., 1997; Bhattacharya, 2019)) or negatively affect other areas of life (e.g., future alcohol-consumption). The work presented in this thesis therefore has potentially wide-

reaching implications that can help inform policy makers, business, and alcohol consumers to make better decisions around mitigating the negative consequences of alcohol hangover.

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Appendices

Appendix 1: Supplementary Materials for Chapter Six

IAPS images

Two sets of images were created for the emotion regulation task – one for each condition. Presentation of sets were randomised and counterbalanced between the conditions.

Set A:

Negative-Decrease: 2800, 3030, 3051, 9270, 3530, 3064, 6300, 6370, 6510, 6831, 8230, 9050, 9140, 9440, 9571, 9600, 9611, 9920, 9921, 9490

Negative-Look: 3140, 2205, 3160, 3180, 3230, 3250, 6210, 9520, 6260, 6312, 6830, 9007, 9181, 9400, 9420, 9430, 9470, 9570, 9620, 9910

Positive-Increase: 1601, 8500, 8090, 5629, 5623, 8380, 1590, 2650, 5260, 5200, 1620, 5594, 2311, 8496, 2550, 8370, 2000, 2040, 1750, 2530

Positive-Look: 2370, 2352, 8034, 2391, 1540, 8350, 4641, 8461, 1500, 5660, 2341, 8540, 8210, 2091, 7502, 1920, 5830, 5760, 1440, 2050

Neutral-Look: 7175, 7009, 7010, 7950, 7034, 7020, 7185, 7000, 7187, 6150, 5510, 5920, 7182, 5740, 7100, 5530, 2840, 2220, 2850, 2190

Set B:

Negative-Decrease: 2100, 2900, 3000, 3053, 3150, 3190, 3220, 6200, 6252, 6313, 6530, 6550, 9001, 9180, 9265, 3500, 6250, 9530, 9630, 9810

Negative-Look: 2110, 3061, 6211, 3110, 9421, 3300, 3550, 4621, 6360, 6540, 6571, 6610, 9041, 9182, 9220, 9290, 9250, 9410, 9560, 9911

Positive-Increase: 2030, 1740, 2510, 5201, 8180, 5001, 4640, 5891, 5270, 5470, 1600, 1999, 8600, 2540, 1610, 8501, 2260, 8190, 2070, 1710

Positive-Look: 7325, 2340, 1510, 8200, 5000, 8120, 8400, 4603, 1604, 4599, 8490, 4610, 8030, 1463, 5621, 2160, 8420, 2150, 2080, 1460

Neutral-Look: 7217, 5534, 7160, 7090, 2200, 7491, 7006, 7050, 2890, 7235, 7002, 7035, 7640, 2870, 7004, 7080, 7233, 7207, 2880, 5532